IBICS
Irish Biological Inorganic Chemistry Society

UCD DUBLIN

7th Symposium of the Irish Biological Inorganic Chemistry Society (IBICS-7)

Scientific Programme

UCD Village, Dublin | 15th December 2023

Symposium sponsors:

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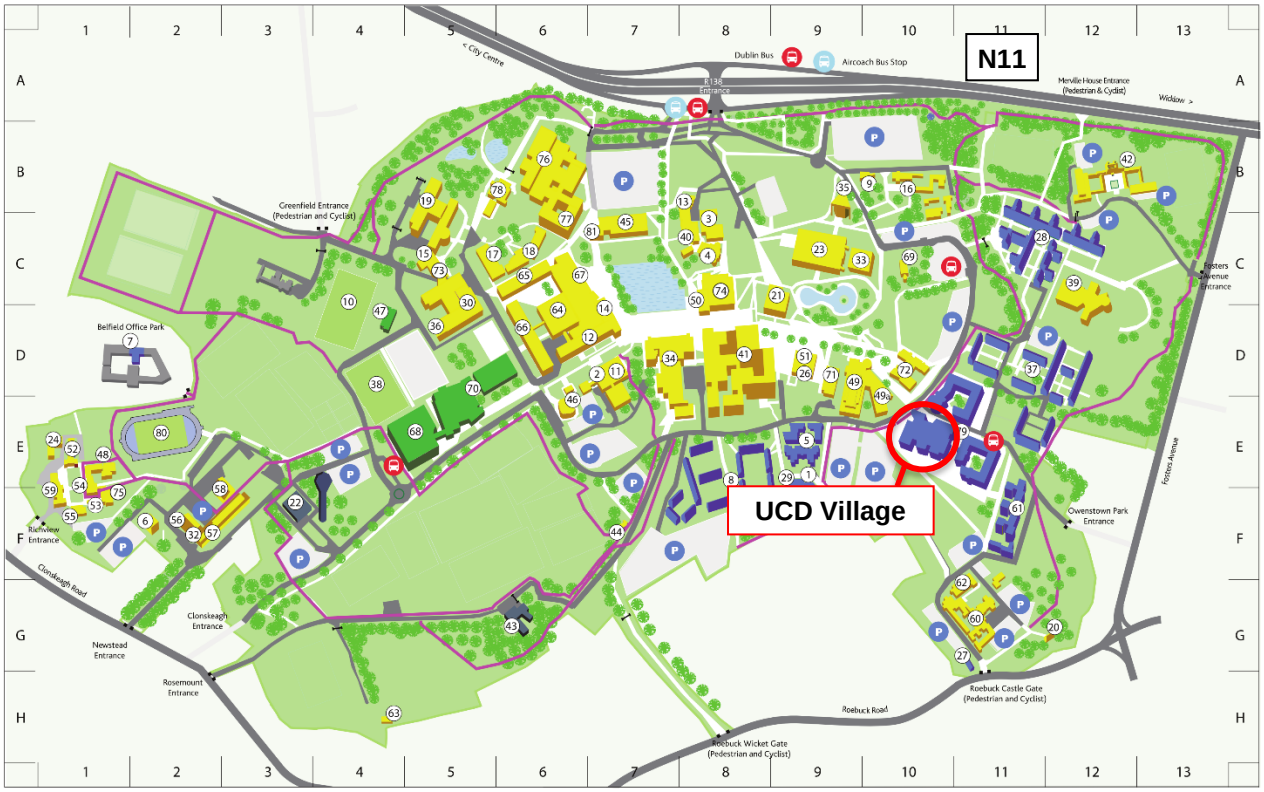
Table of Contents

*7th Symposium of the Irish Biological Inorganic Chemistry Society – **IBICS-7***
Friday, 15th December 2023

Time	Speaker and title of presentation	Code	*Venue*
10:00	Registration, coffee, and poster setup		*Balcony*
10:30	Opening remarks: Professor Michael Devereaux, IBICS President		*Theatre*
	Session 1, Chair: *Dr Luca Ronconi*		*Theatre*
10:40	**Plenary: Professor Ramón Vilar** (Imperial College London) *"Targeting DNA with luminescent metal complexes – imaging and therapy"*	PL1	
11:20	Maria Byrne (University College Dublin): *"Multi Emissive Silica Nanomaterials for DNA Sensing"*	O1	
11:35	Rhianne Curley (Dublin City University): *"Exploring the Efficacy of a Mitochondrial G4-Targeted Ruthenium(II) Complex in Cell Monolayers and Multicellular Tumour Spheroids"*	O2	
11:50	**Invited: Professor Denise Rooney** (Maynooth University): *"Medicinal Applications of Transition Metal Coordination Complexes of N-Based Heterocyclic Derivatives"*	IL1	
12:20	**Flash Session, Chair:** *Dr Andrew Phillips* 3-minute presentations ***sponsored by ICI***	F	*Theatre*
12:35	Lunch (provided) and **Poster Session 1**	P	*Balcony*
13:25	IBICS Annual General Meeting		*Theatre*
	Session 2, Chairs: *Prof. Susan Quinn*		*Theatre*
13:55	**Invited: Professor Mathias Senge** (Trinity College Dublin): *"On Trial: The Case of Aluminum Dipyrrinato Photosensitizers"*	IL2	
14:25	Simon Poole (Dublin City University): *"The Generation of a New Class of Click Chemistry-Derived Di-nuclear Copper(II) Artificial Metallonuclease"*	O3	
14:40	Darren Beirne (Maynooth University): *"Pt(IV)-Sunitinib pro-drug conjugates displaying promising preliminary anti-cancer activity"*	O4	
14:55	Lewis More O'Ferrall (Royal College of Surgeons in Ireland & TU Dublin): *"Ga(III) siderophore complexes - A Metallo-Trojan Horse Strategy to tackle Aspergillus fumigatus lung infections"*	O5	
15:10	Ella O'Sullivan (TU Dublin): *"Investigating Apoptosis Induction as a Mechanism of Action of Novel Metal-Dicarboxylate-Phenanthroline Complexes"*	O6	
15:40	**Poster Session 2, *sponsored by RSC Republic of Ireland Section***	P	*Balcony*
	Session 3, Chair: *Prof. Celine Marmion*		*Theatre*
16:40	Dr Neville Murphy (University of Galway): *"Intracellular behaviour of metallacarboranes through the lens of stimulated Raman spectroscopy"*	O7	
16:55	**Plenary: Professor Petra Heffeter** (Medical University of Vienna) *"Development of new strategies to overcome the therapeutic limitations of inorganic anticancer drugs"*	PL2	
17:35	**Presentation of IBICS Postgraduate Gold Medal** Dr Amir Abdo (CÚRAM/University of Galway) *"Metalloporphyrins as Potential Nitric Oxide Scavengers for treatment of breast cancer"*	GM	
17:55	Prize-giving, and closing remarks by Professor Michael Devereaux		
18:00	**Wine reception**		*Balcony*

IBICS
Irish Biological Inorganic Chemistry Society

WELCOME



LEGEND Student Residences · Sports and Recreation · Education, Research and Innovation · Pedestrian Route · Woodland Walk · Vehicle Route

University College Dublin Campus Regulations

UCD is private property, please respect the grounds and facilities
UCD reserves the right to refuse admission
These premises are covered by the Occupiers Liability Act
Areas of UCD grounds and buildings are covered by CCTV for your safety and security

TRAFFIC

DRIVING:
- Campus Speed limit is 30 km/h
- Vehicles using the campus must comply with the Road Traffic Act
- Coaches may only be brought to campus by prior arrangement with UCD Estate Services

PARKING
- Only permit holders may park in permit parking spaces (applies 8:00-17:00 Mon-Fri, during term time; Sept – May. See website for dates)
- Visitor parking spaces are hourly paid (see signs in car parks for hours when applicable)
- Vehicles may only be parked in designated parking spaces and are parked at owner's risk
- Vehicles left unattended for more than three weeks will be deemed abandoned and may be removed
- Wheel clamping is used to facilitate parking management on campus
- Clamp release fee is indicated by signage in the car parks

TRANSPORT

Bus stops are located at:
- Across from Merville & Glenomena Student Residences (grid C10, buildings 37 & 28)
- To the rear of the UCD Sports Centre (grid E4, building 68)
- At the UCD Village (grid E11, building 79)
- At the R138 entrance (grid B8)

BICYCLES
- Bicycles must be parked in the bicycle racks provided
- Bicycles attached to trees, railings or handrails will be removed
- Bicycles may not be brought into buildings
- Bicycles left unattended for more than three weeks will deemed abandoned and may be removed
- Bicycles are parked at owners risk

RECREATION
- Sports may only be played in designated facilities
- Sports facilitated may be booked through the UCD Sports Centre (grid E4, building 68)
- Dogs must be kept on a leash
- Dog dirt is a health hazard; owners must always clean up after their dogs

PROHIBITED ACTIVITIES
- Skateboarding, rollerblading, BMX Biking, Parkour
- Consumption of alcohol, except in designated areas
- Camping
- Littering
- Dumping: fly tippers will be prosecuted

- UCD is a smoke-free campus.
- Smoking and vaping/e-smoking in all forms is prohibited

COMMERCIAL ACTIVITIES

Prior permission is required for
- The distribution of leaflets, flyers or marketing material
- Photography/filming
- Casual trading

WWW.UCDESTATES.IE/**CAMPUSREGULATIONS**

Building Index

Building Index	No.	Grid
Agnes McGuire Social Work Building	1	E9
UCD Agriculture and Food Science Centre	2	D7
Ardmore Annexe	3	C8
Ardmore House	4	C8
Ashfield Residences	5	E9
Ames Newstead	6	F2
Belfield Office Park	7	D2
Belgrove Student Residences	8	E8
Bicycle Shop	9	B10
UCD Bowl	10	C4
Campus Services	11	D7
UCD Centre for Molecular Innovation and Drug Discovery	12	D6
Centre for Experimental Pathogen Host Research (CEPHR)	13	B8
Centre for Synthesis and Chemical Biology (CSCB)	14	D7
Charles Institute	15	C5
UCD Clinton Centre for American Studies (Belfield House)	16	B10
UCD Computer Centre	17	C5
UCD Computer Science and Informatics Centre	18	C6
UCD Conway Institute	19	B5
Crannóg House	20	G12
Daedalus Building	21	C9
Energy Centre	22	F2
UCD Engineering & Materials Science Centre	23	C9
Environmental Protection Agency	24	E1
UCD Geary Institute (Arts Annexe)	25	F9
Gerard Manley Hopkins Centre (UCD International Office)	26	D9
Glebe House	27	G11
Glenomena Student Residences	28	C11
Hanna Sheehy-Skeffington Building	29	D9
Health Sciences Centre	30	C5
UCD Humanities Institute Ireland	31	F9
Leinster Rugby	32	F2
Irish Institute for Chinese Studies (UCD Confucius Institute)	33	C9
UCD James Joyce Library	34	D7
UCD John Hume Institute for Global Irish Studies (William Jefferson Clinton Auditorium)	35	B9
Medical Bureau of Road Safety (MBRS)	36	D5
Merville Student Residences	37	D11
National Hockey Stadium	38	D4
National Institute for Bioprocessing Research and Training (NIBRT)	39	C12
National Virus Reference Laboratory (NVRL)	40	C8
Newman Building	41	D8
NovaUCD	42	B12
Oakmount Créche	43	G6
UCD O'Kane Centre for Film Studies [Observatory]	44	F7
O'Reilly Hall	45	C7
Our Lady Seat of Wisdom Church	46	E6
Pavillion	47	D4
Planning and Environmental Policy	48	E1
UCD Lochlann Quinn School of Business	49	D9
UCD Moore Centre	49a	D8,UCD
Research	50	C8
Restaurant	51	D9
Richview Buildings Laboratory	52	E1
Richview Lecture Building	53	F1
Richview Library	54	E1
Richview Memorial Hall	55	F1
Newstead Block A	56	F2

Building Index (cont)

Building Index (cont)	No.	Grid
Newstead Block B [Main Bld]	57	F2
UCD Institute of Sport & Health	58	E3
Richview School of Architecture	59	E1
Roebuck Castle	60	C11
Roebuck Hall Residence	61	F11
Roebuck Offices	62	C11
UCD Rosemount Environmental Research Station	63	H4
UCD O'Brien Centre for Science (Hub)	64	D6
UCD O'Brien Centre for Science (North)	65	C6
UCD O'Brien Centre for Science (West)	66	D6
UCD O'Brien Centre for Science (East)	67	C6
UCD Sports Centre	68	E5
St. Stephens	69	C10
UCD Student Centre	70	D5
Building 71	71	D9
UCD Sutherland School of Law	72	D10
Systems Biology Ireland (SBI)	73	C6
Tierney Building (Administration Building)	74	C8
UCD Earth Institute - Richview	75	F1
Veterinary Hospital	76	B6
UCD Veterinary Sciences Centre	77	B6
Woodview House	78	B5
UCD Village	79	E10
Running Track	80	E2
University Club	81	C6

Academic Index

UCD Colleges & Schools - Colláistí & Scoileanna UCD

UCD College of Arts and Humanities

	No.
UCD School of Art History and Cultural Policy	41
UCD School of Classics	41
UCD School of English, Drama and Film	41
UCD School of History	41
UCD School of Irish, Celtic Studies and Folklore	41
UCD School of Languages, Cultures and Linguistics	41
UCD School of Music	41

UCD College of Business

	No.
UCD Michael Smurfit Graduate Business School	
UCD Lochlann Quinn School of Business	49

UCD College of Engineering and Architecture

	No.
UCD School of Architecture, Planning and Environmental Policy	49
UCD School of Biosystems and Food Engineering	23
UCD School of Chemical and Bioprocess Engineering	23
UCD School of Civil Engineering	57
UCD School of Electrical and Electronic Engineering	23
UCD School of Mechanical and Materials Engineering	23

UCD College of Health and Agricultural Sciences

	No.
UCD School of Agriculture and Food Science	2
UCD School of Medicine	30
UCD School of Nursing, Midwifery and Health Systems	30
UCD School of Public Health, Physiotherapy and Sports Science	78
UCD School of Veterinary Medicine	77

UCD College of Social Sciences and Law

	No.
UCD School of Archaeology	41
UCD School of Economics	41
UCD School of Education	62
UCD School of Geography	41
UCD School of Information and Communication Studies	41
UCD School of Law	72
UCD School of Philosophy	41
UCD School of Politics and International Relations	41
UCD School of Psychology	41
UCD School of Social Policy, Social Work and Social Justice	29
UCD School of Sociology	41

UCD College of Science

	No.
UCD School of Biology and Environmental Science	66
UCD School of Biomolecular and Biomedical Science	64
UCD School of Chemistry	72
UCD School of Computer Science	78
UCD School of Earth Sciences	66
UCD School of Mathematics and Statistics	65
UCD School of Physics	65

Campus Information

Services

Bicycle Shop	9	B10
Campus Bookshop	34	D7
Centra Supermarket	79	E10
Copi-Print	34, 41	D7, D8
Laundry	28, 61	C11, F11
Mail Room	56	F2
Pharmacy	70	D5
Sports Centre Barber	68	E5
Student Desk	74	C8
Student Health Service	70	D5
Students' Union	70	D5
Students' Union Shop	22, 34, 64	C9, D7, D6
UCD Hill	62	C11
UCD Village Welcome Desk	79	E10

Gates Opening Times*

R138 Entrance	24 hours
Clonskeagh Entrance, (Mon-Sun)	07.00 - 00.00
Owenstown Entrance (Mon-Sat)	07.00 - 00.00
Fosters Avenue Entrance	07.00 - 00.00
Richview Entrance (Mon-Fri)	07.00 - 00.00
Richview Entrance (Sat)	07.00 - 18.00
Merville House Pedestrian and Cyclist Entrance	07.00 - 00.00
Newstead Gate (Mon-Sun)	24 hours
Roebuck Castle, Pedestrian & Cyclist Entrance	24 hours
Greenfield Park, Pedestrian & Cyclist Entrance	24 hours
Roebuck Pedestrian & Cyclist Entrance (Mon-Fri)	07.00 - 18.00

* gate opening times may change due to Bank holidays or for operational reasons

UCD Contact Centre: (01) 716 7000
UCD Emergency Line: (01) 716 7999

The organisers of today's event would like to thank the following for their generous sponsorship of the Symposium and support of IBICS:

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RSC LOCAL SECTION
REPUBLIC OF IRELAND

Welcome by President of IBICS:

On behalf of the IBICS committee, a very warm welcome to this, the 7th symposium of the Irish Biological Inorganic Chemistry Society (IBICS-7). We look forward to meeting you all on the day and we are extremely grateful and thankful to our colleagues in UCD for organising and hosting the event this year. The Society's mission is to develop, foster and promote a strong national network of scientists collaborating in research areas such as biology, chemistry, physics and medicine with an interest in biological inorganic chemistry. In this regard, the Society, since its establishment in May 2017, has held six successful symposia hosted by MU/DIT, UoG, RCSI and DCU, with two on-line virtual meetings held during the Covid-19 crisis. These annual meetings offer excellent opportunities for members to network and I am delighted to see that a number of very fruitful inter-disciplinary collaborations have evolve as a result, creating opportunities to share expertise and infrastructure.

A key feature of all IBICS symposia is the inclusion of our plenary lectures delivered by distinguished and internationally renowned experts. The IBICS-7 symposium will feature plenary lectures by Professor Ramón Vilar (Professor of Medicinal Inorganic Chemistry, Imperial College London, UK) and Professor Petra Heffeter, (Professor of Applied and Experimental Oncology, Medical University of Vienna, Austria). The programme also includes a number of keynote lectures, alongside a number of oral and flash presentations by early stage researchers and PhD scholars. There will be prizes for both the best student oral and poster presentations.

The presentation of the IBICS Postgraduate Gold Medal award has been a key highlight of the IBICS symposia since 2019. Following an open call, IBICS received a number of excellent nominations this year, and after an independent review and evaluation process we are delighted to announce that the recipient of the award this year will be Dr. Amir Mohammed Abdo (University of Galway). As a biomedical engineer Amir has distinguished himself across a range of criteria throughout his inter-disciplinary PhD which has focused on an in-depth examination of the modification of the hemin structure to synthesise nitric oxide (NO)-scavenging compounds and the fabrication of novel NO-scavenging hydrogels. His research performance, achievements and contributions in the applications of biological inorganic chemistry and his additional professional engagements during his PhD studies are highly commendable, and we congratulate Dr. Abdo as this year's award recipient.

You can find IBICS updates and news on the IBICS website http://ibics.ie and via our Twitter account @IbicsIreland. Please keep us informed of key achievements which we would be more than happy to publicize on the website. Please also consider following us on Twitter!

All members are invited to the IBICS AGM meeting just after lunch (13:25-13:55) and to the reception which will take place immediately after the scientific programme ends.

May we also take this opportunity to acknowledge our sponsors who are listed above in the book of abstracts.

Kind regards,

Professor Michael Devereux, President of IBICS

UCD School Of Chemistry
Scoil na Ceimice UCD

Céad Míle Fáilte go COBÁC - Welcome to UCD

A warm welcome to University College Dublin for the 7th Instalment of the annual Irish Biological Inorganic Chemistry Symposium. This event is growing each year and has become a staple in the calendar of those interested in bioinorganic chemistry, medicinal chemistry, life sciences and the overlaps between these areas. This event has been held in Maynooth, Galway, RCSI, DCU and is now coming to UCD for the first time. We are delighted to welcome you to Belfield and the modern UCD Village venue, surrounded by up-to-date amenities and student residences with views of the Wicklow mountains. In this programme, we have included details about the venue, safety information and how to travel here by public or private transportation. Thank you to the Society for giving us the opportunity to host this year's event and to all the delegates for attending.

On the following pages, we provide the abstracts for all of the speakers and poster-presenters who have accepted the invitation to share their work with the IBICS community. As you can see by leafing through them, there is a great diversity of research at the interface of chemistry, medicine and biology on display and hopefully more fruitful collaborations may arise from the questions and conversations at the symposium. Thanks, in particular, to all the early-career researchers who submitted abstracts for consideration.

We would like to take this opportunity to acknowledge our sponsors: the Institute of Chemistry of Ireland, the Royal Society of Chemistry Republic of Ireland Local Section, Mason Technologies, Merck, GPE and Julabo, and Accuscience - all of whom generously provided financial support without which this event could not have taken place. We would also like to thank ICI, SLS and CRC Press (Taylor & Francis Group) for supporting prizes. I have been very heartened by the enthusiastic support of companies and professional societies across Ireland for this multidisciplinary meeting, and want to express how thankful I am for their gracious support.

Kind regards,

Dr Joseph Byrne
On behalf of the Local Organising Committee

Local Organising Committee: Dr Joseph Byrne (Chair), Assoc. Prof. Susan Quinn, Dr Andrew Phillips, Sophie Kavanagh

General Information

Venue:

The Irish Biological Inorganic Chemistry Society will host its 7th Symposium in the **UCD Village**, University College Dublin, Dublin 4 on Friday December 15th 2023. UCD Village is in the south of the UCD Belfield Campus, Eircode: D04 C1P1. Registration will be held in the UCD Village. Plenary, keynote, and oral lectures, as well as flash presentations, will be held in the **UCD Village Lecture Theatre**, which is upstairs from the foyer of UCD Village.

Poster presentations will take place in the **balcony space**, where coffee and tea will also be served in the morning and afternoon. The lunch break and the wine reception will be hosted in the balcony space. A wide range of food and drink is also available in the Food Hall downstairs in UCD Village. Please visit exhibition tables of our sponsors on the balcony of UCD Village during the breaks.

IBICS AGM:

IBICS AGM will be held at the Symposium, directly after lunch (13:25-13:55) in the UCD Village Lecture Theatre, which is open to all registered IBICS members.

Emergency Procedure:

If an incident or accident occurs during the event, call Campus Services Emergency line 7999 (01 716 7999) and alert one of the organising committee.

Medical Emergency:

If there is a medical emergency on campus that requires an ambulance, the Emergency Campus helpline can be contacted on 01 716 7999.

Fire Safety:

Assembly point for evacuation of UCD Village is Rear of UCD Moore Centre for Business Building (Pavement at Back of Building)

Travel:

UCD Belfield Campus is located beside the N11 in Stillorgan, easily accessible by public transport. This event is being held outside of term, but nonetheless, there is limited parking available. Delegates are encouraged to use public transport where possible.

Car

- Hourly paid car parks are available, but spaces are extremely limited. It is advised to use Public Transport where available. (Map of carpark locations at this link)
- Hourly paid parking operates during the hours 8:00hrs-17:00hrs, Monday – Friday (excluding bank holidays).

Train

- Arriving at **Heuston Station** please find the bus stop for the 145 bus. Take the 145 bus in the direction of Ballywaltrim, alighting at the UCD bus stop, which is a 10-minute walk from the Belfield campus.
- Arriving at **Connolly Station** please continue on to Pearse Street Station. Directly outside Pearse Street station there are a selection of buses going directly to UCD.

Bus

- The bus routes that serve UCD are: 145, 155, 39a, 46a, X25, X27, 164, 824, X28, 32X, 7B, 7D, 27X, 41X, 46E, 47, 116, 118, 142, 180, 845, X30, S4, S6

DART:

- The closest stop is **Booterstown,** which is a 20-minute walk to UCD
- Alternatively, you can alight at **Sydney Parade**, where there is a shuttle bus service to UCD that operates between the hours of 8-10am and 4-6pm. There is a charge of €1 per trip, payable to the driver.
  Timetable available here: https://ucdestates.ie/commuting/getting-here/shuttle/
- Coming from **Blackrock Station**, the frequent S6 bus serves UCD Village directly.

Luas:

- The closest Luas stop to UCD is **Windy Arbour**, which is a 30-minute walk from the Belfield campus. This stop is on the Green Line service of the Luas.

More information available at: https://ucdestates.ie/commuting/

Internet:

The “UCD Wireless” network and “eduroam” network are available on campus. Details at: https://www.ucd.ie/itservices/ourservices/networkinfrastructure/wirelessservices/

Registration fees

The symposium is open and free to all IBICS members. For non-members, the registration fee is the cost of the annual membership. Fees are €30 for academics, €20 for postdocs and €10 for postgraduate/undergraduate students. For any queries, please contact the IBICS treasurer at treasurer@ibics.ie.

Presentations:

Plenary speakers will have 40 minute slot for their lecture, Invited speakers will have 30 minutes and oral presenters will have 15 minutes available. All speakers are asked to keep a few minutes free at the end of their presentation for questions. Speakers are requested to check in with their session's chairperson in advance of the session, and provide a copy of their presentation to be loaded onto the podium computer, or to test their own computer. If any presenters would like their lecture recorded, for their records or for sharing, this can be arranged. Flash presenters will have 3 minutes to present 1-2 slides, which should be provided to the organisers in advance.

Poster presenters are asked to set up posters during the morning registration (10:00-10:30) or any time before the first poster session at 12:30. The poster boards will be located at the balcony space in UCD Village. There will be a prize awarded to the best poster and there will also be a prize for best flash presentation, which is a chance for presenters to advertise their poster and its key findings. Thanks to the Royal Society of Chemistry for sponsoring the poster presentation event, and also thanks to the Institute of Chemistry Ireland for sponsoring the flash presentations.

Prizes:

Prizes will be awarded to the **best poster**, **best flash presentation** and **best oral presentation** (by a graduate student). The oral presentation prize is sponsored by IBICS, the flash prize is sponsored by silver-tier sponsor, the Institute of Chemistry of Ireland, and the poster prize is sponsored by Scientific Laboratory Supplies (SLS). All three prize-winners will be presented with a copy of "Targeted Metallo-Drugs: Design, Development, and Modes of Action" (Edited by Etelka Farkas & Celine J. Marmion) courtesy of the kind sponsorship of CRC Press – Taylor & Francis Group.

Prize sponsors:

Symposium Sponsors:

Plenary Lecturers – Speaker Profiles

Ramon Vilar is a Professor of Medicinal Inorganic Chemistry and Vice-Dean for Research at the Faculty of Natural Sciences at Imperial College London. He was previously Director of the Institute of Chemical Biology (2019-23) and Director of Research in the Chemistry Department (2015 to 2023). His PhD (supervised by Prof Mingo, FRS – 1993 to 1996) focused on the synthesis and catalytic applications of palladium clusters. This was followed by 2 years postdoctoral research on supramolecular chemistry and molecular recognition of metal complexes. He was appointed Lecturer in Chemistry at Imperial College in 1998. Between 2004 and 2006 he was Group Leader at the Institute of Chemical Research of Catalonia (ICIQ), returning to Imperial College as a Senior Lecturer in 2006. Between 2009 and 2015, he held an EPSRC Leadership Fellowship to study the chemical biology of non-canonical DNA structures. Currently his group works in two broad research programs: **i)** Chemical Biology and Medicinal Chemistry (e.g. development of probes for non-canonical nucleic acids; understanding the aggregation of amyloids; phototoxicity of metal complexes); **ii)** Environmental chemistry (e.g. developing new materials for the removal of pollutants from water; probes for toxic species).

Petra Heffeter is a Full Professor at the Center for Cancer Research (Medical University of Vienna, Austria) in the area of applied and experimental oncology.

Regarding her education, she is a cancer biologist as well as toxicologist and has habilitated in 2015 for which she was honoured with the Otto-Kraupp Habilitation Award. Her research focusses on the investigation of mechanisms underlying the resistance and responsiveness of cancer cells to therapy and has been used for the design of several new anticancer (pro)drugs. One of these projects allowed the design of a novel albumin-targeted platinum drug (Albuplatin), which is currently developed towards clinical phase I evaluation. For her research, over the years Petra received several innovation awards. In total, she has published 155 manuscripts (~6,000 citations). Moreover, she is coordinator of a research group, co-coordinator of the Doc-Funds project “International PhD Programme: Translational Oncology '' and has in total secured >€5 million third-party funding.

Invited Lecturers – Speaker Profiles

Denise Rooney is the Head of the Department of Chemistry and Associate Dean of the Faculty of Science in Maynooth University. Her PhD focused on Time-Resolved Raman spectroscopy and Photolysis of Transition Metal-Carbene Complexes, completed in 1991 under the supervision of Prof John McGarvey at Queens University in Belfast. Following from this, she carried out post-doctoral research at the University of York with Prof Robin Perutz (FRS). She was appointed as a lecturer in inorganic chemistry at Maynooth University in 1994. Her research focuses on Metal Complexes and Materials Chemistry, more specifically the antimicrobial properties of novel metal complexes. She was awarded the Dean of Graduate Studies Doctoral Supervision Award in 2019.

She was elected as the Associate Dean of the MU Faculty of Science and Engineering in 2019 and she was appointed as Head of Department of Chemistry in 2020.

Mathias Senge is Chair of Organic Chemistry at Trinity College Dublin. After completing his PhD thesis in plant biochemistry in 1989 under the supervision of Prof. Horst Senger in Marburg, he continued on to complete a postdoctoral fellowship with Prof Kevin M. Smith at UC Davis. Following this, he received his habilitation in Organic Chemistry in 1996 at the Freie Universität Berlin. He was a Heisenberg fellow at the Freie Universitat Berlin and UC Davis and also held visiting professorships at Griefswald and Potsdam,. He was appointed Professor in Organic Chemistry at Universität Potsdam in 2002 and took up the Chair in Organic Chemistry at Trinity in 2005.

He was the recipient of fellowships from the Studienstiftung des Deutschen Volkes and the Deutsche Forschungsgemeinschaft and from 2005-2009 he was a Science Foundation Ireland Research Professor. Recently he was awarded a Senior Hans Fischer Fellowship at the Institute of Advanced Studies of the Technical University Munich.

His research interests include the chemistry and biochemistry of tetrapyrroles, synthetic organic chemistry, photobiology, crystallography and medicinal and bioorganic chemistry.

Plenary, Invited and Award Abstracts

(PL, IL, GM)

(PL1) Targeting DNA with luminescent metal complexes – imaging and therapy

Prof Ramon Vilar [a]

[a] *Imperial College London*

Abstract

Non-canonical DNA structures (such as triplex and quadruplex DNA) have been shown to form in vivo and play important biological roles. Thus, there is increasing interest in developing small molecules that can interact selectively with a given DNA topology for either imaging or therapy. An area of particular interest is the design and development of metal complexes that can selectively bind to guanine-quadruplex DNA (G4 DNA). These non-canonical DNA structures have been proposed to be involved in transcription, telomere maintenance and replication, and therefore have been identified as attractive anticancer drug targets. This lecture will discuss some of our work on imaging G4 DNA in cells[1,2] as well as how light can be used to modulate and control the cellular properties of small molecules. [3,4]

References:

[1] *Angew. Chem. Int. Ed.* **2023**, *62*, e202310402 (DOI: 10.1002/anie.202310402)
[2] *Nat. Commun.* **2021**, *12*, 162 (DOI: 10.1038/s41467-020-20414-7)
[3] *Angew. Chem. Int. Ed*. **2021**, *60*, 10928–10934 (DOI: 10.1002/anie.202100151)
[4] Preprint: ChemRxiv (10.26434/chemrxiv-2023-rt8kr)

(PL2) Development of new strategies to overcome the therapeutic limitations of inorganic anticancer drugs

Prof Petra Heffeter [a,b]

[a] Center of Cancer Research and Comprehensive Cancer Center, Medical University of Vienna, Austria; [b] Interuniversitary Research Cluster „Translational Cancer Therapy Research", University of Vienna and Medical University of Vienna

Abstract

Despite all recent therapeutic developments, cancer is still among the main causes of human death. The major problems of the used anticancer drugs are adverse effects and therapy resistance. In order to improve the tumor specificity of the currently available treatment, the characteristic conditions of the malignant tumor need to be exploited. To this end, the research cluster „Translational Cancer Therapy Research" follows diverse strategies.

In this talk selected examples will be presented such as novel inhibitors of the epidermal growth factor receptor (EGFR), which are activated using a cobalt-based prodrug concept by the characteristic hypoxic conditions of the malignant tissue. Moreover, albumin-targeted therapeutics will be presented which exploit not only the enhanced permeability and retention (EPR) effect (comparable to nanoformulations) but also the cancer cell-specific needs for enhanced nutrient supply. One lead candidate of the research cluster is the ruthenium compound BOLD-100, which is currently in clinical phase II testing. In addition, platinum(IV)-based maleimide-targeted prodrugs are preclinically developed, which show promising anticancer activity in vivo. Noteworthy, in addition to cancer cells also specific aspects of the tumor microenvironment are targeted by our latest multi-action prodrug systems, where additional bioactive moieties (e.g. indoleamine 2,3-dioxygenase inhibitors) are attached.

(IL1) Medicinal Applications of Transition Metal Coordination Complexes of N-Based Heterocyclic Derivatives

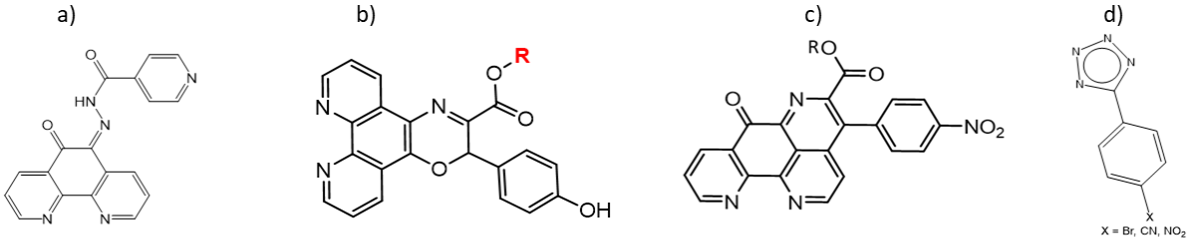
D. Rooney,[a,b] F. Heaney,[a,b] , C. Evans,[a,b] , S. Ward,[a,b], M. Ahmed,[a,b] M. McCann,[a] M. Butler,[b,c] K. Kavanagh [b,c]

[a]Maynooth University, Department of Chemistry, Co. Kildare (Ireland); [b]Maynooth University, Kathleen Lonsdale Institute for Human Health Research, Co. Kildare (Ireland); [c]Maynooth University, Department of Biology, Co. Kildare (Ireland); denise.rooney@mu.ie

Abstract

Infectious diseases caused by bacteria have been a leading cause of mortality worldwide, with diseases such as tuberculosis (TB) infecting 33% of global population in its latent form.[1] Discovery of penicillin in 1928 heralded the development of a wide range of therapeutics to target bacterial illnesses, leading to the "antibiotic era".[2,3] However, the development of resistant strain of bacteria has left humanity yet again facing bacterial infections of multi drug resistant (MDR) strains, demanding the discovery of therapeutics of higher efficacy. Globally, more than 300 million people suffer a serious fungal infection causing over 1,350,000 deaths each year.[4] *Candida* is a leading cause of healthcare-associated bloodstream infections in US hospitals.[5] Some types of *Candida* are becoming increasingly resistant to first- and second-line antifungals. Our group focuses on metal complexation of appropriate ligands with the aim of achieving synergistic effects; displaying efficacy greater than that of ligands and metal centres combined.

The presentation will describe, the synthesis, solution characteristics and antimicrobial activity of silver complexes of the derivatives of phenanthroline ligands (Figure 1a) and (Figure 1b). The synthesis and characterisation and biological properties of rhenium carbonyl complexes of (Figure 1b and 1c) and of cyclopentadienyl iron carbonyl complexes of tetrazoles (Figure 1d) will also be described.



R= methyl, propyl, hexyl

Figure 1

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(IL2) On Trial: The Case of Aluminium Dipyrrinato Photosensitizers

M. O. Senge,[a]

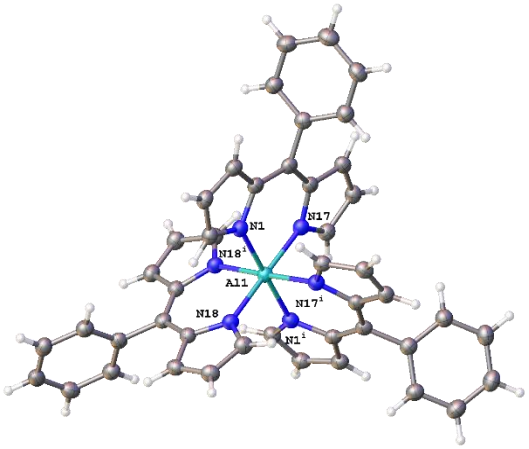
[a]*Trinity College Dublin, The University of Dublin, School of Chemistry, Dublin (Ireland)*

Abstract

Photodynamic therapy (PDT) is a non-invasive targeted therapy which involves systemic or topical administration of a drug, a so-called photosensitizer (PS), which after irradiation of a specific wavelength of light is excited and reacts with the coexisting molecular oxygen. As a result, highly reactive singlet oxygen and other reactive oxygen species (ROS) can be formed leading to specific cell death of cancer cells or antimicrobial effect against bacteria or viruses.[1]

The current clinically approved PSs, mainly porphyrinoids (*e.g.,* Foscan),[2] for anti-cancer PDT still encounter drawbacks (*e.g.,* poor water solubility, aggregation, photobleaching, slow clearance from the body, *etc*.); thus, it is important to discover alternative PSs. Metal coordinated complexes that form metal-to-ligand charge transfer (MLCT) excited states have gained significant attention over the past years (*e.g.,* ruthenium, boron, gallium, or iridium complexes).[3] Metals from group 13 of the periodic table coordinated with dipyrrins have been reported. Nevertheless, aluminum complexes have not yet been investigated in terms of photophysical or photobiological properties towards a photodynamic effect. Aluminum is abundant, inexpensive, and widely used like an adjuvant in vaccines.

We have developed novel *tris*-dipyrrinato aluminum complexes with different substituents at the 5-position of the dipyrrin core and focused on the photophysical properties upon photoexcitation and the influence of the metal coordination center by comparison with related In, Ir, Ga, and Fe complexes.[4,5] In addition, we investigated the electronic effects of the withdrawing or donating groups to the dipyrrin core; the singlet or triplet intraligand state ability; their emissive properties; and their triplet excited states properties.



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IBICS Postgraduate Award Lecture:

(GM) Metalloporphyrins as Potential Nitric Oxide Scavengers for treatment of breast cancer

Amir M. Abdo Alsharabasy,[a] Sharon Glynn,[b] Pau Farràs,[c] Abhay Pandit[a]

[a]CÚRAM, SFI Research Centre for Medical Devices; [b]Discipline of Pathology, Lambe Institute for Translational Research, School of Medicine; [c] School of Biological and Chemical Sciences, Ryan Institute, University of Galway

amir.abdo@universityofgalway.ie

Abstract

In breast cancer, nitric oxide (•NO) orchestrates the angiogenesis and lymphangiogenesis processes within the tumour microenvironment, depending on its concentration, duration of exposure, and the surrounding tissue.[1,2,3] These are essential for supplying oxygen and nutrients to the tumour tissue and spreading breast cancer cells. More importantly, the surrounding cells' sensitivity to •NO varies with its concentrations.[1,3] Scavenging •NO is a potential strategy to restore these cells' homeostasis. To achieve that, hemin, known as one of the efficient scavenging compounds for NO,[4,5] was modified for the synthesis of a number of more stable hemin conjugates and their NO-scavenging efficiency was evaluated at the cellular levels.[6] These compounds included hemin-tyramine, hemin-tyrosine, hemin-tyrosine dipeptide and hemin-styrene conjugates. The intracellular •NO was detected using Diaminofluorescein-FM diacetate (DAF-FM-DA), where a concentration dependent inhibition for the fluorescence signal corresponding to •NO was observed following the treatment of MDA-MB-231 cells with DETA-NONOate, as a •NO-donor. However, the concomitant cell treatment with these different compounds decreased the intracellular levels of •NO, dependent on the concentration and type of compound. Similarly, the NO-scavenging was tested using iNOS-transfected HCC1806, where the highest •NO-scavenging potency was observed in case of hemin-styrene. The decrease in these intracellular •NO levels was accompanied with inhibition of cell migration, tested via scratch assay and transwell migration assay. Moreover, the different hemin conjugates except hemin/styrene, in spite of working as •NO-scavenging compounds, caused enhancement of protein nitration. This was evidenced from the increased expression of nitrotyrosine, due to the nitrite release in the presence of oxygen following the reduction of Fe(III) to Fe(II). The mechanism of hemin-induced-protein nitration was also studied by a number of cell based and cell-free studies, which explained how the different compounds modulate the •NO-enhanced nitration of cellular proteins. To summarize, the study introduced a novel class of iron-based •NO-scavenging compounds, which were synthesized using straightforward procedures and possessed unique chemical properties. Furthermore, the synthesized compounds exhibited diverse abilities to regulate TNBC cell migration and blood vessel dilation, each with distinct molecular effects at the cellular level.

Acknowledgements

This work was supported by a research grant from Science Foundation Ireland (SFI), co-funded under the European Regional Development Fund under Grant number 13/RC/2073_P2 and the College of Engineering and Informatics Scholarship Scheme, University of Galway, Ireland.

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Oral Abstracts

(O)

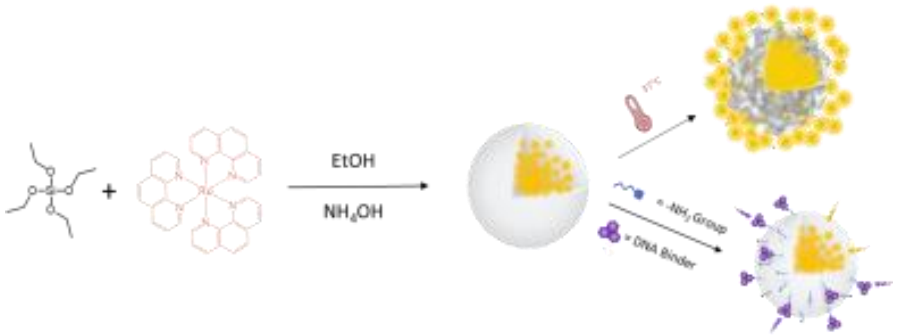
(O1) Multi-Emissive Silica Nanomaterials for DNA Sensing

Maria H. Byrne and Susan J. Quinn

School of Chemistry, UCD, Dublin, Ireland; maria.byrne.3@ucdconnect.ie

The properties of nanomaterials including controllable size, morphology,surface functionality and biostability make them attractive for biological applications, from drug delivery to biosensing to cellular imaging. Silica nanoparticles (SiO_2 NPs) present an ideal candidate for such applications due to their facile synthesis, encapsulation with target molecules, controlled stability and their bioavailability[1,2]. DNA, an important diagnostic and therapeutic target, can be specifically targeted by SiO_2 NPs through their known affinity for DNA and through the encapsulation of DNA targeting metal complexes into the NPs[3]. SiO_2 NPs smaller than 100 nm are optimally scaled for controlling parameters such as cellular interactions, biocompatibility and controllable dissolution[4].

In this work, the encapsulation of a ruthenium polypyridyl complex into Stöber type[5]SiO_2 NPs of varying size, conveys optical properties to the nanoparticles and establishes trackable materials for sensing applications. Functionalization of the SiO_2 NPs surface offers further control of their cellular interactions and stability, while establishing anchors for subsequent modifications. Therefore, these SiO_2NPs can function as delivery systems through enhancing their dissolution susceptibility, triggering release of the internalized complex. The time and temperature dependent dissolution of these emissive SiO_2 NPs has been tracked via electron microscopy and optical spectrometry.



The subsequent modification with luminescent DNA probes to the surface of emissive SiO_2 NPs produces multi emitting, DNA binding systems with the capacity for multiple sensing events and trackability in cells. These DNA probes, with highly conjugated structures, can also function as hosts to complimentary molecules through non-covalent interactions. This produces a second and independent delivery and release mechanism
to these SiO_2 NPs, via surface interactions.

This nanoparticle system could greatly enhance the pharmaceutical efficacy of drugs, the sensitivity of biosensors and the success of biomedical therapies.

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(O2) Exploring the Efficacy of a Mitochondrial G4-Targeted Ruthenium(II) Complex in Cell Monolayers and Multicellular Tumour Spheroids

R. C. Curley,[a] L. Holden,[a] G. Avella[a] and T. E. Keyes[a]

[a] *Dublin City University, National Centre for Sensor Research, School of Chemical Science, Dublin (Ireland); rhianne.curley2@mail.dcu.ie*

Abstract

Ruthenium(II) polypyridyl complexes are emerging probes for cellular imaging and are also under investigation for their phototherapeutic potential. Mitochondria, essential cellular organelles, are an important target for therapeutic intervention, as the centre of cellular respiration. There is growing evidence supporting presence of mitochondrial guanine quadruplexes (mitoG4s) in the mitochondrial genome, and their influence on cellular functions. [1] However, there are few probes reported to date that are specifically designed to target these features. Closing this gap is crucial to achieving a more comprehensive understanding of the role played by mitoG4s in cellular functions.

In this contribution, the *in-vitro* behaviour of a novel G4-targeting ruthenium complex, Ru-TAP-PDC3, is explored. The phototherapeutic potential of this complex was assessed in HeLa and HEK-293 (human embryonic kidney) cell monolayers, and in HeLa multicellular tumour spheroids (MCTS). Ru-TAP-PDC3 undergoes photoinduced electron transfer under normoxic and hypoxic conditions, generating a selective light activated therapeutic that targets mitoG4s and mitochondrial DNA (mtDNA). Binding studies indicate this ruthenium complex shows high affinity to mitoG4s and mtDNA. After a 24-hour incubation with the complex, localization occurs within the mitochondria of live HeLa cells, where our studies indicate that mtDNA is depleted, mitochondrial potential is reduced, caspase activation occurs, and apoptosis is induced. These results suggest that Ru-TAP-PDC3 is an outstanding candidate for phototherapy and can be activated in both normoxic and hypoxic cellular environments, leading to programmed cell death.

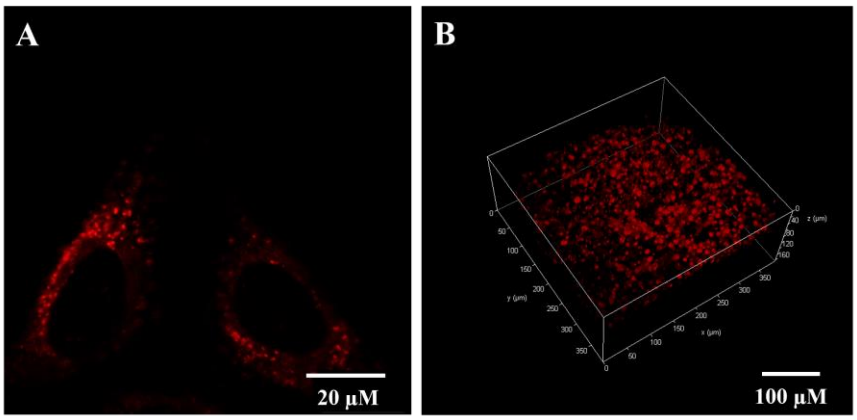

Figure 1 (a) Ru-TAP-PDC3 (50 µM, 24 h) in HeLa cell monolayers and **(b)** in HeLa spheroids (100 µM, 24 h)

Acknowledgements

Science Foundation Ireland (SFI) grant number 18/EPSRC-CDT/3585 and 19/FFP/6428 and the Engineering and Physical Sciences Research Council (EPSRC) EP/S023321/1

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(O3) The Generation of a New Class of Click Chemistry-Derived Di-nuclear Copper(II) Artificial Metallonuclease

Simon Poole, Joseph Hennessy, Georgia Menounou, Bríonna McGorman & Andrew Kellett[1]

[1] *SSPC, the SFI Research Centre for Pharmaceuticals, School of Chemical Science, Dublin City University, Dublin 9 (Ireland)*

simon.poole4@mail.dcu.ie

Abstract

Common cancer therapeutics such as cisplatin are highly effective at crosslinking neighbouring guanine residues on B-DNA duplexes. However, resistance mechanisms and high toxicity associated with platinum therapeutics has motivated researchers to develop new treatments involving polynuclear metal complexes. One successful example is BBR3464[1], a cationic polynuclear platinum agent capable of long-range crosslinking interactions that circumvent typical 1,2-di-adduct repair processes. Here, we have employed a copper-catalysed azide-alkyne cycloaddition (CuAAC) approach[2,3] to generate a new class of bis-phenanthroline copper(II) complex. Thus, these agents were designed to promote long-range DNA cleavage via two distal copper(II) coordinated phenanthroline residues with the aim of overcoming limitations associated with the repair of localized DNA damage. Commercially available di-alkynes with varying linker lengths and modifications were selected to enable a DNA damage structure-activity-relationship study from the resultant complexes. From the library of compounds generated, one lead agent called BPL-C6 was identified (Figure 1A). The complex can selectively bind and cleave AT rich DNA from the minor groove at low micromolar concentrations and has promising selective anticancer activity.

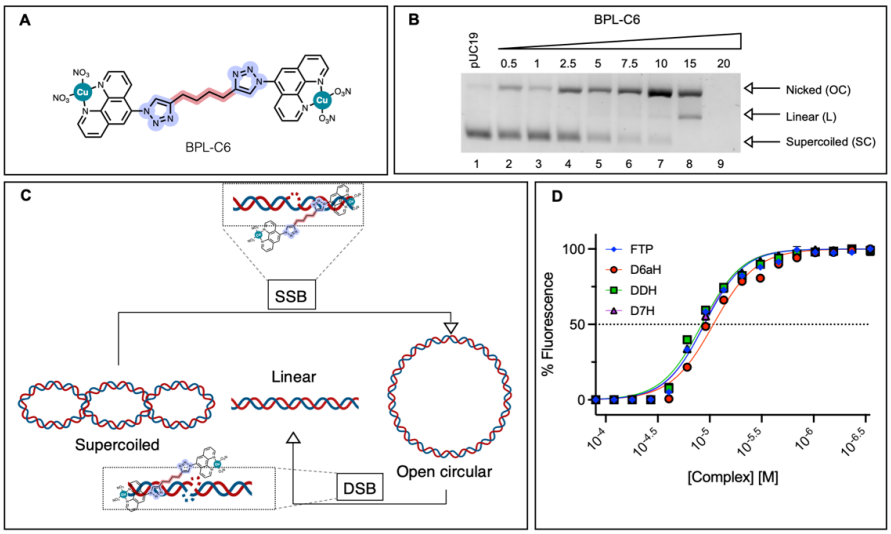

Figure 1: **A** Molecular structure of the artificial metallonuclease, BPL-C6. **B** Cleavage profile of BPL-C6 towards supercoiled pUC19 DNA. **C** Schematic of the conversion of supercoiled pUC19 DNA to open circular and linear forms. **D** DNA binding analysis with four fluorescently tagged DNA hairpins of varying AT and GC content using microscale thermophoresis.

Acknowledgements

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(O4) Pt(IV)-Sunitinib pro-drug conjugates displaying promising preliminary anti-cancer activity

Darren Fergal Beirne,[a] Orla Howe,[b,c] Eithne Dempsey,[a]
Trinidad Velasco-Torrijos,[a,d] Diego Montagner[a,d]

[a] Maynooth University, Department of Chemistry; [b] Technological University Dublin-City Campus, School of Biological and Health Sciences, Dublin, Ireland; [c] Technological University Dublin-City Campus, Centre for Biomimetic and Therapeutic Research, FOCAS Research Institute, Dublin, Ireland; [d] Maynooth University, Kathleen Lonsdale Institute for Human Health Research, Ireland. darren.beirne.2017@mumail.ie

Abstract

Tyrosine Kinases (TKs) are enzymes whose actions are the transfer of a phosphate group from Adenosine Triphosphate (ATP) specifically to the tyrosine residues of cellular targets. TK's are promising targets in oncology as they play a major role in cell regulation pathways and their expression/mutation is often the major cause of increased cellular proliferation. For example, overexpression of Platelet Derived Growth Factor Receptor (PDGFR), one such TK, is associated with angiogenesis and metastasis in many tumour tissues. Sunitinib Malate, approved for treatment against renal cell carcinoma, is regarded as a multi-tyrosine kinase inhibitor due to its inhibition of multiple TK's, including, but not limited to PDGFR, Vascular Endothelial Growth Factor Receptor and c-KIT. Our recent review shows that Sunitinib-metal drug conjugation as a valuable strategy to overcome cancer cell drug resistance/healthy cell toxicity[1]. One key discovery is that Sunitinib has displayed synergistic activity when used in combination with cisplatin in different tumour types[2]. Recently, we have developed Pt(IV)-Imatinib/Nilotinib conjugates that displayed improved activity in Neuroblastoma relative to conventional chemotherapy of Imatinib with cisplatin[3]. Here, we report the progress of the development of Pt(IV)-Sunitinib pro-drug conjugates based on the scaffolds of three FDA approved Pt(II) chemotherapeutics: cisplatin, oxaliplatin & carboplatin. Reduction studies of the complexes via ^{1}H NMR and Cyclic Voltammetry are shown followed by their preliminary cytotoxicity against cancer cell lines overexpressing c-Kit/PDGFR/VEGFR, including prostate/breast cell lines.

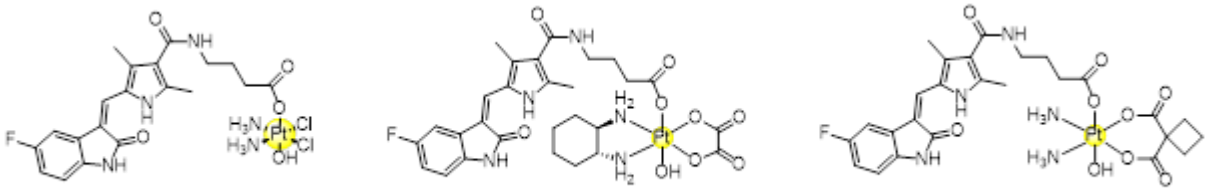

Figure 1. Structures of cisplatin/oxaliplatin/carboplatin based Pt(IV)-Sunitinib conjugates.

Acknowledgements
Funding of this research by Irish Research Council via a Government of Ireland Postgraduate Scholarship (GOIPG/2020/55)

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(O5) Ga(III) siderophore complexes - A Metallo-Trojan Horse Strategy to tackle *Aspergillus fumigatus* lung infections

L. More O'Ferrall[1,2,3], B. Grassiri[4,6], M.E. Piatek[3,5], J.A. Sake[4], S. Esin[7], G. Batoni[7], C. Ehrhardt[4], K. Kavanagh[3,5], A.M. Piras[6], A.M. Healy[3,4], C. O'Connor[2], D.M. Griffith[1,3]

[1]Department of Chemistry, Royal College of Surgeons in Ireland, Dublin 2, Ireland; [2]School of Food Science and Environmental Health, Technological University Dublin, City Campus, Ireland; [3]SSPC, The Science Foundation Ireland Research Centre for Pharmaceuticals, Ireland; [4]School of Pharmacy and Pharmaceutical Sciences, Trinity College Dublin, Dublin 2, Ireland; [5]Department of Biology, Maynooth University, Maynooth, Ireland; [6]University of Pisa, Department of Pharmacy, 56126 Pisa, Italy; [7]Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, 56126 Pisa, Italy

Lewismoreoferrall@rcsi.com

Abstract

In 2019, 4.95 million deaths were associated with the global rise in antimicrobial resistance (AMR), with lower respiratory infections being the most problematic cohort accounting for more than 1.5 million deaths. This highlights the urgent need to develop novel antibiotics as AMR is reported to be one of the leading causes of death worldwide.[1] The World Health Organization has categorized *Aspergillus fumigatus* (*A. fumigatus*) in the critical priority group of fungal pathogens associated with serious risk of mortality and morbidity in humans.[2] *A. fumigatus* is the most common fungus isolated from cystic fibrosis (CF) patients. This is of high concern as invasive aspergillosis is associated with a mortality rate of between 40 and 90% in the immunocompromised.[3] An emerging approach to fight microbial infections is to exploit nutritional vulnerabilities such as Iron (Fe). Bacteria have a high demand for Fe as it plays a vital role in multiple cellular processes. Gallium (Ga^{3+}) shares many chemical and physical properties to that of Fe^{3+} and is well known to exhibit antimicrobial properties.[4] Targeting bacterial siderophore Fe-uptake systems is an effective strategy to enhance the intracellular delivery of toxic payloads.[5]

A novel gallium siderophore-based therapy has been formulated to enable efficient delivery to the lungs as a dry powder inhaler (DPI) formulation or a solution for nebulization. The novel formulations have been shown to be selectively toxic against *A. fumigatus*, and non-toxic to NCl-H441 cells. All GaS1 formulations were shown to be suitable for pulmonary drug delivery, and the solution was effective in an in vitro lung infection model mimicking the conditions found in the CF airways. The novel gallium siderophore formulations that efficiently deliver the siderophore-gallium complex to the lungs could be a promising adjuvant therapy for the treatment of *A. fumigatus* infections, also in extreme conditions for CF patients.

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(O6) Investigating Apoptosis Induction as a Mechanism of Action of Novel Metal-Dicarboxylate-Phenanthroline Complexes

Ella O'Sullivan[a,b], Denis O'Shea[c], Michael Devereux[d], Orla Howe[a,b,d]

[a]School of Biological, Health and Sports Sciences, Technological University Dublin, Dublin (Ireland); [b]Environmental Sustainability and Health Institute, Technological University Dublin, Dublin (Ireland); [c]School of Food Science and Environmental Health, Technological University Dublin, Dublin (Ireland); [d]The Centre for Biomimetic and Therapeutic Research, Technological University Dublin, Dublin (Ireland); Email: C16376506@mytudublin.ie

Abstract

A range of Cu(II), Mn(II) and Ag(I) metal complexes incorporating bridging dicarboxylate and chelating 1,10-phenanthroline ligands have been investigated, as potential anti-cancer therapeutic agents, using *in vitro* and *in vivo* models to establish their cytotoxic efficacies[1,2,3]. The preliminary results from these studies suggest that this class of complex offers a range of multi-modal cytotoxic species and that there may be different regulated cell-death (RCD) pathways induced by the complexes contingent upon the type of metal-center present. We hypothesized that the copper complexes apparently apoptosis[4], the manganese analogues may induce autophagy[5], and the silver versions ostensibly stimulate immunogenic or immune-related cell death modalities [2].

The current research project aims to expand our knowledge of the anti-cancer potential of this class of metal complex, further elucidating their cytotoxic mechanisms via an examination of additional potential cellular modes of action using MCF-7 (breast) and HaCaT (normal keratinocyte) cells. Initial cytotoxicity screening showed that all of the metal-dicarboxylate-phenanthroline complexes exhibited superior cytotoxicity when compared to their non-phenanthroline containing precursors, with a variance in the levels of potency observed depending on the type of metal center present. Unlike the Ag(I) analogues, which were previously found to exhibit cellular antioxidant capabilities, the Cu(II) and Mn(II) complexes were found to generate cytotoxic levels of intracellular reactive oxygen species (ROS).

To further explore the regulated cell-death (RCD) pathways an in-depth investigation of apoptosis induction by each complex was performed using the Annexin V/Propidium Iodide assay, followed by quantitative reverse transcription PCR (qRT-PCR) with SYBR Green to establish a panel of apoptotic genes stimulated by each complex. This has established that apoptosis plays an important role as a regulated cell-death mechanism induced by all of metal-dicarboxylate-phenanthroline complexes but of varying significance. Further work will be undertaken to explore the role of the complexes in other regulated cell-death (RCD) pathways and established Raman spectroscopic methods will also be employed to further study the modes of action of the complexes in cells.

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(O7) Intracellular behaviour of metallacarboranes through the lens of stimulated Raman spectroscopy

N. Murphy,[ac] W.J. Tipping,[d] Y. Ding,[e] R. Dwyer,[bc*] K. Faulds,[d] A. Pandit,[c] D. Graham,[d] H. P. Spaink,[e] P. Farràs [ac*]

[a] University of Galway, School of Biological and Chemical Sciences, Ryan Institute, Galway (Ireland); [b] University of Galway, School of Medicine, Lambe Institute for Translational Research, Galway, (Ireland); [c] University of Galway, Science Foundation Ireland (SFI) Research Centre for Medical Devices (CÚRAM), Galway (Ireland); [d] University of Strathclyde, Department of Pure and Applied Chemistry, Technology and Innovation Centre, Glasgow, (United Kingdom); [e] Leiden University, Institute of Biology Leiden, Leiden, (The Netherlands).

Abstract

Previous advancements in multispectral imaging of cells have been primarily in fluorescence microscopy, with up to seven fluorescent signals being unmixed from within the same sample.[1] However, this requires chemical labelling of cellular components which alters the subject of the imaging and has broad spectral frequencies of ~1500 cm^{-1} which can lead to signal overlap and poor signal-to-noise. The comparably narrow spectral frequency (~15 cm^{-1}) of Raman spectroscopy, combined with high spatial resolution and fast image acquisition associated with stimulated Raman spectroscopy (SRS) presents a higher compatibility with complex cellular imaging, especially in the case of multiplex detection of reporters.[2] This work utilizes three different Raman reporters containing C–D, B–H and C≡C functional groups, the signals of which can be readily unmixed using spectral phasor analysis of hyperspectral SRS images.[3] The B–H stretch in metallacarboranes is detected at ~2500 cm^{-1}, which is within the 'cell-silent' window (~1800-2800 cm^{-1}) of the Raman spectrum. This makes SRS an ideal candidate for label free tracking of metallacarboranes within several cell lines.

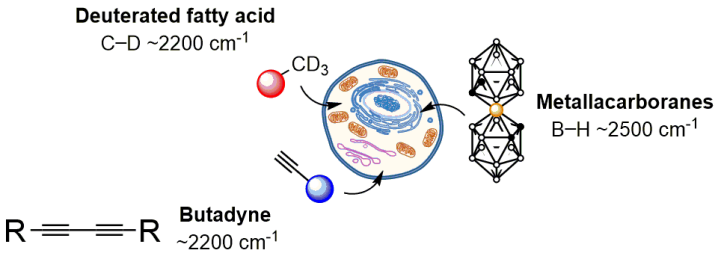

Figure 1: C–D, B–H and C≡C functional groups may be tracked efficiently within the cell label-free using SRS and spectral phasor analysis.

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Poster Abstracts

(P, F)

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Irish Biological Inorganic Chemistry Society

List of Poster and Flash Presentations

Poster Number	Flash	Presenter(s)	Abstract Title
1		Sachidulal Biswas (TCD)	A Structural and Functional Mimic of The P680 Dimer Radical Cation
2	✓	**Federica Brescia (UoG)**	Rational design of gold(III)-glycoconjugates as antiviral agents against SARS-CoV-2
3	✓	**Agnideep Das (TCD)**	Bioinspired Catalytic Oxidative C*(sp3)*-H Fluorination Through Reactive High Valent Cobalt-Fluoride Intermediate
4	✓	**Clara Evans (MU)**	Developing Novel Re(I) tricarbonyl Complexes as Antimicrobial and Anticancer Agents to Combat Drug Resistance
5		Judit Fodor (TCD)	Structure Activity Studies of Bio-active TM-polypyridyl Compounds with Asymmetric bipyridine ligands
6		Daniel Graczyk (UCD)	Synthesis, Characterisation & DNA Binding Interactions of Ru(II)-Pteridinyl Complexes
7	✓	Sophie Kavanagh and **Thomas Rabbitte (UCD)**	Dual Activity Mechanically Interlocked Systems as Antimicrobial Candidates
8		Agnieszka Kawalerska (TUD)	Exploring cyclodextrin-folate derivatives as encapsulation vehicles for the targeted delivery of cytotoxic inorganic metal complexes into folate-expressing cancer cells
9		Oscar Kelly (TCD)	Model Compounds for the Investigation of Electrostatic Effects in Photosynthetic Pigments
10		Darragh McHugh (UoG)	Advancing Cancer Treatment: Zinc-based nanoMOF Unveils Unprecedented Drug Loading of Doxorubicin with Integrated Multimodal Bioimaging Capabilities
11	✓	**Phillip Morgenfurt (DCU)**	Ultrafast light switch properties of $[Ru(phen)_2(dppz\text{-}PDC_3)]^{4+}$
12	✓	**Joshua Thorogood (TCD)**	Synthetic Magnesium Tetrapyrrole Radicals for Mechanistic Studies of Photosystem II
13		Kaja Turzanska (RCSI)	Copper (II) compounds as antimicrobials for the treatment of wound infections
14	✓	**Eleanor Windle (UCD)**	The photophysical study of DNA Binding Phthalocyanine as Combined Photothermal and Photodynamic Therapeutic Agents
15		Karolina Wojtczak (UoG)	The Lanthanide Detective: The Hunt for Unlabelled Lectins and Antiadhesive Antimicrobials
16		Clara Zehe (UCD)	Spectroscopic study and DNA binding of luminescent carbon dots

(P1) A Structural and Functional Mimic of The P680 Dimer Radical Cation

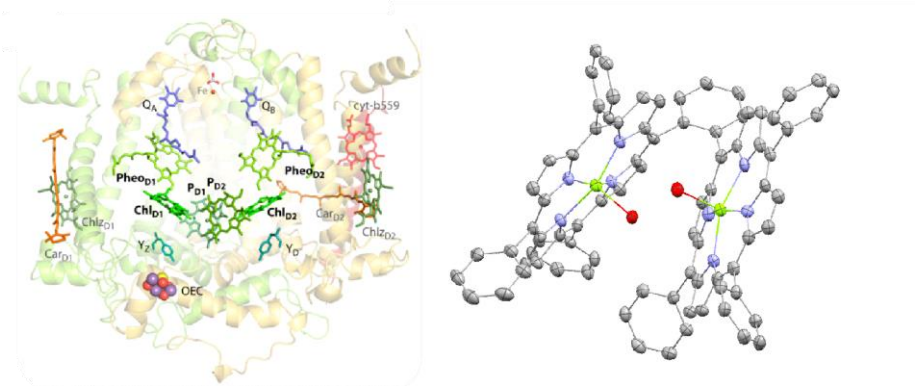
S. Biswas,[a] A. R. McDonald[a]

[a]*School of Chemistry, Trinity College Dublin, The University of Dublin,*

College Green, Dublin 2, Ireland
email: sabiswas@tcd.ie

Abstract

P680, a unique type of chlorophyll a (Chla), serves as photosystem II's main electron donor.[1] According to the PS II X-ray structures, the donor site's D1/D2 core contains four Chla molecules distributed evenly across its center.[2] The central pair of Chl are aligned parallel to each other with a distance of (3.3-3.5 Å), which allows for π–π interaction. However, there is a lack of knowledge regarding $P680^{\bullet+}$, the active oxidant that is considered to be the most potent oxidant in biology. The P680 radical cation has a midpoint potential of ($P680/P680^{\bullet+}$) ≈ 1.1 – 1.3 V vs. SHE.[3] By contrast, the redox potential of Chla has been shown to be 0.78 V vs SHE, whereas the redox potentials of the other well-characterized Chl primary electron donors, P700 and P870, are substantially lower at 0.49 V and 0.45 V vs. SHE, respectively.[4-5] It is unclear how a Chl-based oxidant may achieve such high potentials, and the function of single or multiple Chl units in P680 is still unknown.



Herein, we wish to present the synthesis, characterization and reactivity studies of a structural and functional mimic of the $P680^{\bullet+}$ dimer radical cation. A dimeric magnesium porphyrin has been synthesised to mimic the dimeric core of P680. The dimeric cation radical has been prepared by chemical oxidation from the corresponding Mg-porphyrin dimer. The cation radical was characterized by various spectroscopic methods (EPR, UV-Vis, FTIR, ESI-MS). The reactivity of the generated radical cation towards different phenols have been presented which mimics oxidation of tyrosine by $P680^{\bullet+}$ in PS II.

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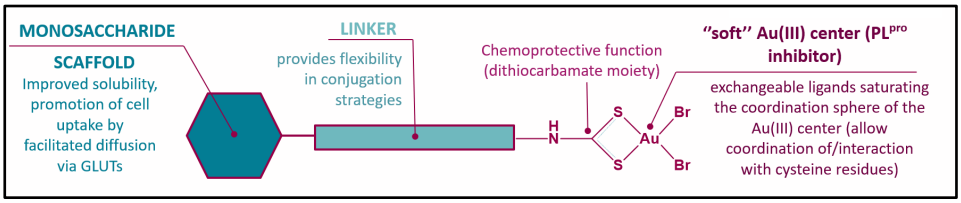
(P2) Rational design of gold(III)-glycoconjugates as antiviral agents against SARS-CoV-2

F. Brescia,[a] L. Ronconi*[a]

[a]*University of Galway, School of Biological and Chemical Sciences, Galway (Ireland);*
f.brescia1@universityofgalway.ie

Abstract

First identified in Wuhan (China) in December 2019, the Coronavirus Disease 2019 (COVID-19) pandemic has been causing a major global health (and, subsequently, socio-economic) emergency which undoubtedly exposed the fragility of the current globalized society. Remarkably, it was the third recent coronavirus-related outbreak after SARS-CoV (2002) and MERS-CoV (2012), thus highlighting the urgent need for dedicated antiviral therapeutics,[1] not an easy task given their extremely low approval rates.[2] Although substantial efforts in drug design and repurposing have been undertaken, to date there are only a few drugs (which were already marketed) have been officially approved for the treatment of COVID-19 infection, mostly recommended to treat patients at high risk.[3]



In this context, metal derivatives are generally under-represented in the compound libraries used for screening in drug discovery campaigns, despite the growing evidence of their role in medicinal chemistry. On account of the aforementioned considerations, based on solid encouraging preliminary results recently obtained in our group,[4] we here report on the design of monosaccharide-containing gold(III)-based derivatives as antiviral agents against Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). The goal is to generate non-toxic gold-glycoconjugates to be taken up by coronavirus-infected cells and, once internalized, capable of acting as potent inhibitors of specific SARS-CoV-2 target proteins, such as the Papain-like Protease (PL^{Pro}). This protease not only orchestrates key processes in viral reproduction but also plays a strategic role in subverting the host's immune response upon viral infection. Furthermore, the conserved nature of PL^{Pro} across the Coronavirus family suggests that targeting this protease may offer a broad-spectrum solution against current and future coronavirus threats.[5]

Acknowledgements

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(P3) Bioinspired Catalytic Oxidative C(*sp3*)-H Fluorination Through Reactive High Valent Cobalt-Fluoride Intermediate

Agnideep Das,[a] Aidan R. McDonald[a]

[a] *School of Chemistry and CRANN/ AMBER Nanoscience Institute, Trinity College Dublin, The University of Dublin, Dublin 2, Ireland, dasag@tcd.ie*

Abstract

An ongoing interest in oxidizing a wide range of hydrocarbons into functionalized raw materials has attracted researchers' attention of finding highly reactive oxidant. Presently, fluorinated and/or chlorinated hydrocarbons have very broad applications in chemical, pharmaceutical and material industries.[1–3] Currently, fluorination of hydrocarbons requires harsh reaction condition (high temperature and pressure, use of super acids, cracking etc.) or limitation in using of fluorine gas, HF, XeF2 and hypofluorites. These conditions are often non-selective and generate undesirable chemical waste with energy, financial and environmental cost.[4] However, biological non-heme halogenase enzyme perform oxidative chlorination of hydrocarbons through an iron metal center, which is cheap and naturally abundant. This halogenation reaction proceeds via an iron(IV) reactive intermediate, which acts as the oxidant. Bioinspiration has led many research groups to synthesize earth abundant high valent metal oxidant, but cobalt centric oxidative fluorination is not well investigated so far.[5–7] Our previous reports evidenced of high valent nickel(III) and iron(IV) fluorides are the reactive oxidant for fluorinating hydrocarbons.[8,9] Both Ni(III) and Fe(IV)-fluorides are capable of rapid fluorination but effective only to weak C-H bonds. Here we investigated a cobalt(II) complex with a tetradentate polyamine ligand scaffold (N,N'-dimethyl-N,N'-bis(2-pyridylmethyl)ethane-1,2-diamine) [**BPMEN**] that can fluorinate stronger C(*sp3*)-H bonds [BDE_{C-H}> 80 kcal/mol] efficiently reacting with selectcfluor™, (1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate)) an electrophilic fluoride source. Further investigation shows the fluorination reaction is catalytic achieving multiple TON of the product formation. Our current investigation reveals that **Co-BPMEN** complex follows bioinspired non-heme halogenase enzyme type mechanism with hydrogen atom transfer (HAT) by reactive high valent cobalt to generate alkyl radical followed by halogen atom transfer (XAT).

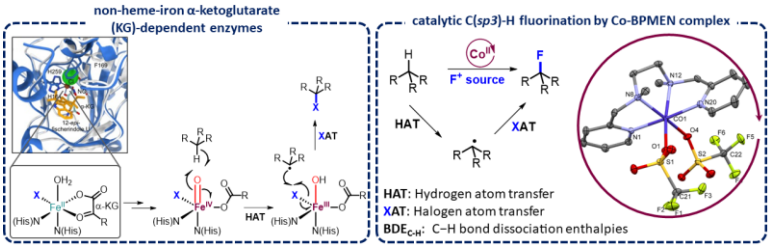

Figure 1: Catalytic radical halogenation mechanism in non-heme-iron α-ketoglutarate (KG)-dependent enzymes (left); bioinspired catalytic fluorination by **Co-BPMEN** complex (right).

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(P4) Developing Novel Re(I) tricarbonyl Complexes as Antimicrobial and Anticancer Agents to Combat Drug Resistance

C. Evans,[a,b] D. Rooney,[a,b] F. Heaney,[a,b] M. McCann,[a] M. Butler,[b,c] K. Kavanagh [b,c]

[a]Maynooth University, Department of Chemistry, Co. Kildare (Ireland); [b]Maynooth University, Kathleen Lonsdale Institute for Human Health Research, Co. Kildare (Ireland); [c]Maynooth University, Department of Biology, Co. Kildare (Ireland); clara.evans.2017@mumail.ie

Abstract

The World Health Organization (WHO) has declared that Antimicrobial Resistance (AMR) is one of the top ten threats facing humanity. AMR is predominantly caused by the misuse or overuse of antimicrobial drugs. Similarly, resistance to commonly used anticancer treatments including cisplatin is also prevalent. This is hugely concerning given that the WHO has said that 1 in 2 people are predicted to be diagnosed with cancer in their life. Clearly new therapeutics with unique modes of action are needed to combat drug resistance.

Previously our group have described the syntheses of two novel classes of phenanthroline ligands, phenanthroline-oxazine and pyrido-phenanthrolinone (**Figure 1 a** and **b**). [1] The latter is structurally related to ascididemin, an alkaloid found in nature that is cytotoxic to cancer cells. [2] My research is centred on the development of carbonyl rhenium complexes incorporating these ligands for their use in different medicinal applications. Tricarbonyl complexes of rhenium are particularly attractive due to their very low *in vivo* toxicity [3] and they have previously been evaluated as anticancer and antimicrobial agents. [4] This presentation will include work on the synthesis, and characterisation of a series of tricarbonyl rhenium complexes in which the lipophilicity of the phenanthroline ligand is altered by increasing the length of the alkyl chain R (methyl, ethyl, propyl or hexyl) (**Figure 1 c** and **d**). The activity of the complexes and the corresponding free ligands were studied against *S. aureus,* MRSA, *C. albicans* and ovarian cancer cells.

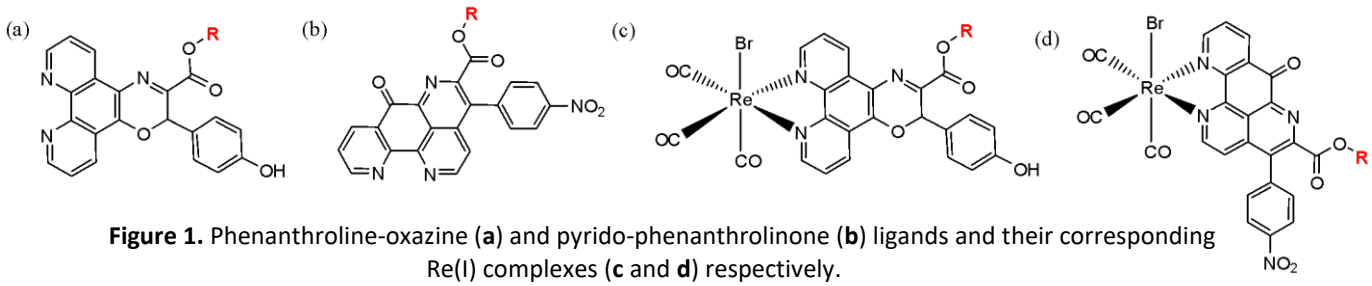

Figure 1. Phenanthroline-oxazine (**a**) and pyrido-phenanthrolinone (**b**) ligands and their corresponding Re(I) complexes (**c** and **d**) respectively.

Acknowledgements

We gratefully acknowledge the Irish Research Council for funding this project. (GOIPG/2020/1448)

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(P5) Structure Activity Studies of Bio-active TM-polypyridyl Compounds with Asymmetric bipyridine ligands

J. Fodor,[a] L. Hallen, M. R. Lawlor,[a] V. Becker,[b] E. M. McGarrigle,[b] S. M. Draper[a]

[a]*School of Chemistry, Trinity College Dublin, D2, (Ireland);*

[b] *School of Chemistry, University College Dublin, Belfield, D4, (Ireland); fodorj@tcd.ie*

Abstract

Transition metal (TM) complexes possess key photophysical properties – they often have intense emission, and long-lived triplet states - making them excellent candidates as photosensitisers (PSs) in triplet-triplet annihilation upconversion (TTA-UC), singlet oxygen generation and photodynamic therapy (PDT). The optoelectronic properties of the metal centre and the chromophore can be modulated through careful ligand design, which has been the central strategy to tune the emissive properties of the metal complexes in the Draper group.[1]

We present here a complex family incorporating unsymmetrical donor/acceptor bipyridine ligands utilising the Os/Ru(II) polypyridyl and Ir(III) cyclometalated frame (**Figure 1**). The effects of different metal centres, as well as the influence of the counter ions (Cl^- vs PF_6^-) on the photophysical properties were evaluated. The three Ru(II) compounds have long emission wavelengths, high quantum yields of emission and show solvent-dependent excited state behaviours. Overall, a significant influence of the metal centre was observed, with both Ir(III) and Os(II) compounds exhibiting a red-shifted emission. Subtle influence of the counterions was also observed, where the Cl salt of the complex had blue-shifted excitation and red-shifted emission wavelength. This family of complexes demonstrate the potential of systematically tailored ligands and complex structures to explore structure-activity relationships in TM complexes.

Preliminary in vitro cell studies have shown that the compounds have moderate cytotoxicity and can generate ROS.

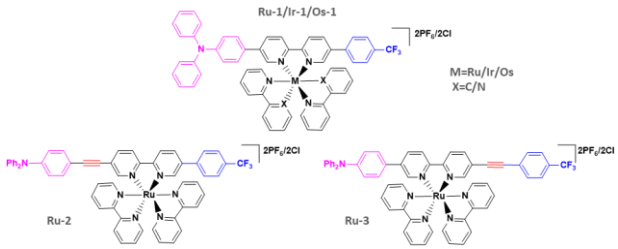

Figure 1. Structures of TM complexes incorporating asymmetric bpy ligands.

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(P6) Synthesis, Characterisation & DNA Binding Interactions of Ru(II) – Pteridinyl Complexes

D. Graczyk,[a] S. J. Quinn[a]

[a]*University College Dublin, School of Chemistry, Belfield, Dublin 4 (Ireland); daniel.graczyk@ucdconnect.ie,*

Abstract

G-quadruplexes (G4) are non-canonical DNA structures composed of stacked guanine tetrads, with influence over transcription regulation and act as potential therapeutic targets for cancer treatment.[1] Ruthenium polypyridyl complexes have been extensively investigated as biomolecular probes due to their versatility and favourable photophysical properties.[2] In this work, two new ruthenium(II) polypyridyl complexes containing an extended pteridinyl ligand with end-groups capable of facilitating hydrogen bonding interactions have been synthesised, characterized, and their enantiomers resolved by chiral column chromatography.[3] The complexes' interactions with double-stranded and guanine-rich DNA have been evaluated. Tuning of the ancillary ligands (phen *vs.* TAP) allows access to luminescent probe and photo-oxidation functionality respectively.[4][5] These complexes have been synthesised with a view to profile their hydrogen bonding interactions and binding specificity to G4 structures.

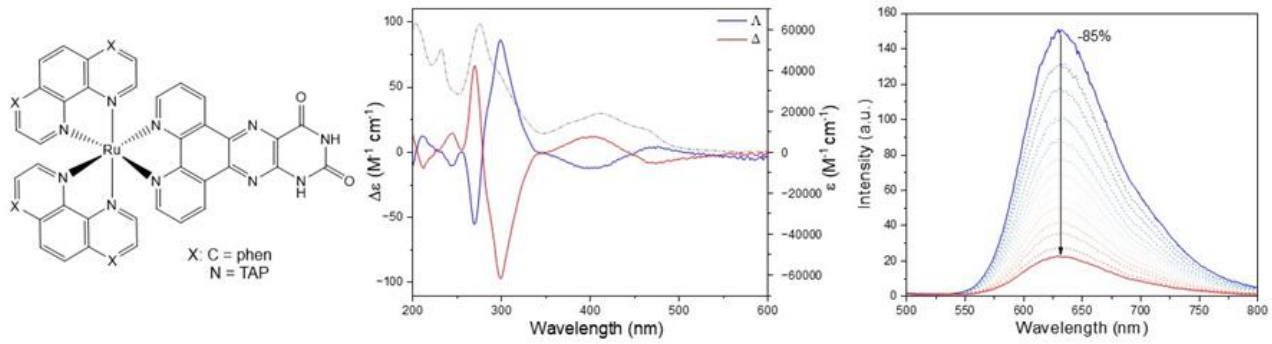

Figure 1. Structure of representative complex, circular dichroism spectra of enantiomers of $[Ru(TAP)_2(L\text{-allox})]^{2+}$ complex, and emission titration of complex *vs.* poly(G) single-stranded nucleic acid, exhibiting emission quenching behaviour.

Acknowledgements

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(P7) Dual Activity Mechanically Interlocked Systems as Antimicrobial Candidates

S. Kavanagh, T. Rabbitte, Joseph P. Byrne

University College Dublin, School of Chemistry, Dublin (Ireland); Conway Institute for Biomolecular and Biomedical Sciences, UCD, Dublin (Ireland)

thomas.rabbitte@ucdconnect.ie , sophie.kavanagh1@ucdconnect.ie

Abstract

Antimicrobial resistance and hospital-acquired infections are emerging global challenges to human health and wellbeing. *Pseudomonas aeruginosa* is a bacterium that is of great concern, having recently been announced as a critical-priority pathogen by the World Health Organisation[1,2]. *Pseudomonas aeruginosa* causes chronic lung infections and is detrimental to immunocompromised people. One of the ways *Pseudomonas aeruginosa* evades the immune system and traditional antibiotic treatments is through the growth of biofilm in chronic infections, governed by characteristic lectin proteins, namely LecA and LecB, which are carbohydrate-based proteins[3]. This project sets out to design self-assembled dual-active mechanically interlocked systems involving carbohydrate-based targeting and bioactive or imaging metal complexes, in order to target these lectins. Using sugars to target lectins is an area of interest in this project, since lectins are a conserved component of the bacterium[3]. This strategy can prevent infection or be used in tandem with antimicrobial agents and re-sensitise the pathogen to them. This also allows for a more selective approach, which is important when using metallo-drugs that can cause toxicity anywhere in the host. Mechanically interlocked molecules are useful as they are biologically robust and resistant to degradation[4]. The Byrne Research group has shown some of the first examples of using metal-coordination chemistry in tandem with sugars to prevent biofilm formation without having bactericidal effects[5]. To date, several potential self-assembled mechanically interlocked molecule precursors have been explored, stemming from simple chemical transformations including amide couplings and Click chemistry. A library of modular components will be constructed which can be used in different combinations to give rise to varying functionality and utility. This strategy will allow tuning of selectivity and activity by screening of complementary components of the interlocked systems.

Acknowledgements

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(P8) Exploring cyclodextrin–folate derivatives as encapsulation vehicles for the targeted delivery of cytotoxic inorganic metal complexes into folate-expressing cancer cells

A. Kawalerska[a], P. McCarron[b], M. McCann[c], M. Devereux[d], M. Mcnamara[e] and O. Howe[b]

[a]School of Biological, Health, and Sports Sciences, Technological University Dublin, Dublin (Ireland); [b]School of Chemical and Biopharmaceutical Science, Technological University Dublin (Ireland); [c]Department of Chemistry, Maynooth University, Kildare (Ireland); [d]The Centre for Biomimetic and Therapeutic Research, Technological University Dublin, Dublin (Ireland); [e]Graduate Research School, Technological University Dublin, Dublin (Ireland)

Abstract

Folate, also known as vitamin B9 is essential for one-carbon transfer reactions in nucleic acid synthesis, DNA replication, cellular growth and division and it is therefore essential for rapidly growing cancer cells. Folate enters cells via the folate receptor (FR) and reduced folate carrier (RFC) shown to be over-expressed in certain cancer tissues (epithelial breast, ovarian, and lung cancer) compared to normal tissue and therefore can be exploited as a drug delivery target[1]. Research at TU Dublin has been carried out on derivatives of oligosaccharides containing folate/folic acid attached to β Cyclodextrin (CDEnFA) and its inclusion complexes involving anti-folates such as methotrexate (MTX) (CDEnFA:MTX). It was found that the addition of folate to the CDEn significantly increased the delivery/efficacy of the MTX drug in a range of cancer cells[2-3]. A range of silver(I), copper(II), and manganese (II) complexes incorporating dicarboxylate and 1,10-phenanthroline (phen) ligands (metal-dicarboxylate-phen) have been previously synthesised in this laboratory which display potent cytotoxicity towards a range of cancer cell lines[4].

This new research project seeks to explore the use of appropriate cyclodextrin folate/folic acid derivatives (CDEnFA) similar to those previously studied to generate inclusion species of selected metal-dicarboxylate-phen complexes to target the folate receptor in high folate expressing epithelial breast, ovarian, and lung cancer cell lines. Inhibitors of the Folate receptor (FR) and reduced folate carrier (RFC) will be used to determine the mode of action and efficacy of the targeted CDEnFA-(metal-dicarboxylate-phen) inclusion complexes. CDEnFA and the inclusion complex of CDEnFA:MTX will also be tested in parallel on the same cell lines and in the same conditions.

The objective is to determine if this approach can significantly improve the delivery, efficacy and selectivity of the metal-dicarboxylate-phen complexes into cancer cells that overexpress the folate receptor (FR), the reduced folate carrier (RFC) and also the Proton-coupled Folate Transporter (PCFT)). It is anticipated that this research will also provide further insights into the cellular signalling pathways of drug delivery through folate mechanisms.

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(P9) Model Compounds for the Investigation of Electrostatic Effects in Photosynthetic Pigments

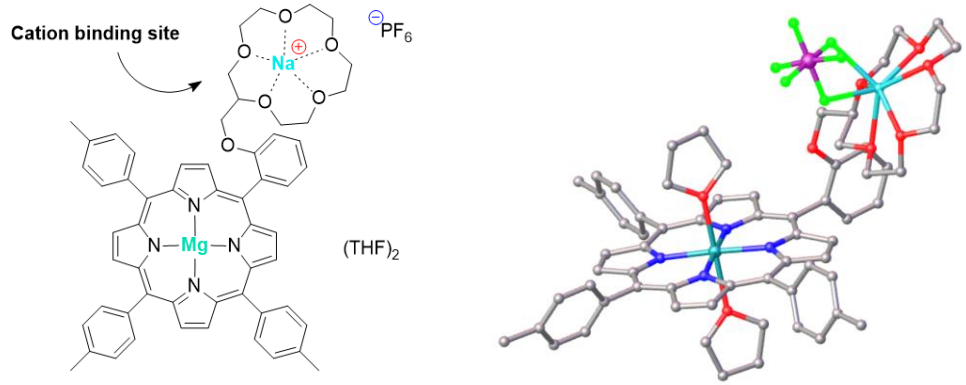
Oscar Reid Kelly, Brendan Twamley and Aidan R. McDonald

School of Chemistry, Trinity College Dublin, The University of Dublin, Dublin 2, Ireland

email: kellyos@tcd.ie, aidan.mcdonald@tcd.ie

Photosynthetic water oxidation is catalysed by the enzyme Photosystem II (PSII). The reaction is initiated by 1-electron photo-oxidation of a chlorophyll-*a* tetramer named P680. The product is a π-cation radical complex, $P680^+$, with an exceptionally high redox potential of 1.1 - 1.3 V vs SHE. This species drives water oxidation by oxidising the oxygen evolving complex *via* a tyrosine residue.[1] The extreme redox potential of $P680^+$ renders it the most potent oxidant in biology, a fact that is especially interesting considering the comparatively diminished redox potentials of monomeric chlorophyll-*a* and other related photosynthetic pigments (0.45 - 0.78 V vs SHE).[1, 2] The origin of the high redox potential of $P680^+$ is unknown, but a number of proposals have been put forward in the literature, such as: the nature of axial ligands at Mg, the relationship between different chlorophyll molecules in the pigment, and the electrostatic/dielectric environment of the surrounding protein.[3, 4, 5] Uncovering the factors that contribute to the high reactivity of $P680^+$ promises to both improve our understanding of water oxidation in PSII and unearth new design principles for synthetic oxidation catalysts.

This work aims to address the last of the above-listed postulates by demonstrating the impact of electrostatic interactions on the redox and reactivity properties of chlorophyll model compounds. To this end, we have synthesised and characterised novel crown ether appended Mgporphyrins, their adducts with redox-inactive metal cations and their 1 electron oxidation products in the presence/absence of bound cations.



Chlorophyll model compound

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(P10) Advancing Cancer Treatment: Zinc-based nanoMOF Unveils Unprecedented Drug Loading of Doxorubicin with Integrated Multimodal Bioimaging Capabilities

D. McHugh,[a] M. Winterlich,[a] C. Papatriantafyllopoulou [a]

[a]*School of Biological and Chemical Sciences, College of Science and Engineering, University of Galway, H91 TK 33 Galway, Ireland.*

d.mchugh13@universityofgalway.ie

Abstract

Metal organic frameworks (MOFs) have attracted considerable attention in recent years because of their applicability in the environmental, industrial and biomedical fields. In cancer research, there is a pressing need for innovative drug delivery systems due to limitations in conventional treatments, such as systemic toxicity and inadequate targeting. The quest for novel platforms is driven by the urgency to enhance therapeutic efficacy while minimizing side effects. Advanced systems, like biocompatible nanoMOFs with high drug loading, offer a promising solution by providing improved precision, multifunctionality, and controlled release mechanisms. These advancements represent a transformative shift in cancer therapy, holding the potential to revolutionize treatment approaches.[1-3]

Here, a novel biocompatible nanoMOF with rhombohedral morphology based on a multitopic elongated carboxylate linker, $[Zn_4O(L'H_3)]_n$ is synthesised solvothermally and characterised.

By UV-Vis, the nanoMOF was determined to have high doxorubicin loading and toxicological evaluation of the organic linker, OnG7, and Dox@OnG7 was conducted using the HDF cell line. At concentrations ranging from 0.5 to 1 µM, both the organic linker and OnG7 demonstrated non-toxic properties, aligning with the administered dosage of Dox. Remarkably, the cytotoxic impact of Dox@OnG7 indicated that the MOF exhibits a protective effect on healthy cells, mitigating the toxicity of Dox in comparison to its nonencapsulated form.

Acknowledgements

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(P11) Ultrafast light switch properties of $[Ru(phen)_2(dppz\text{-}PDC_3)]^{4+}$

P. Morgenfurt,[a] A. Chettri,[b] B. Dietzek-Ivanšić,[b] Lorcan Holden,[a] T. E. Keyes[a]

[a]Dublin City University, School of Chemical Sciences, Dublin (Ireland); [b]Friedrich Schiller University Jena, Institute of Physical Chemistry, Jena (Germany)

Abstract

Ruthenium(II) complexes containing dppz = dipyrido[3,2-a:2′,3′-c]phenazine ligands behave as optical switches emitting from non-aqueous media with emission extinguished in water, attributed to water driven switching of the location of the excited state.[1] This effect is operational on DNA binding as DNA binding excludes water, switching emission on and has been widely studied solution and recently demonstrated to be active in live cells when the complex is targeted to the nucleus.[2] Thus such light switches offers opportunities for detection and imaging of DNA in-cellulo and many Ru-dppz complexes have been shown to show comparable affinity for B DNA as ethidium bromide (EB).

Some Ru dppz complexes have been shown to associate with high affinity and exhibit light switch effect on binding to non-canonical forms of DNA however, given the similarly high affinity for duplex, there is little opportunity for discrimination in cellulo. We recently prepared a novel complex, comprising the Ru(II) dipyridylphenazine complex with well-known G4 selective ligand Phen-DC3, one of the most well known G-Quadruplex stabilizers, into a single structure that shows high and preferential association with G4 DNA. More importantly, it offers clear discrimination between DNA and G4 on the basis of emission lifetime data.[3] Here the time-resolved photophysical properties of this complex, $[Ru(phen)_{2(}dppz\text{-}PDC_3)]^{4+}$, are investigated streak camera lifetime measurements, and a combination of femtosecond and nanosecond pump-probe spectroscopy, with interpretation supported by steady state spectroelectrochemistry.

Steady state and time resolved measurements in water and acetonitrile confirm light switch properties similar to $[Ru(phen)_2(dppz)]^{2+}$ are retained, but with additional charge transfers occurring leading to a new excited state properties. Using fs transient absorption (fsTA) spectroscopy, a Jablonski diagram for the electronic states upon photoexcitation at 410 nm was deducted. Studies were then carried with bound complex to multiple G4 topologies with clear discrimination in behaviour on DNA binding and between duplex and G4 DNA, based on binding affinity and emission lifetime.

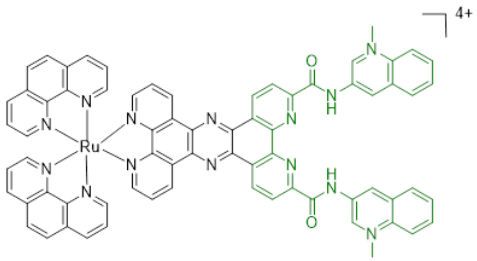

Figure 1. Structure or $[Ru(phen)_2(dppz\text{-}PDC3)]^{4+}$. The attached PDC3 moiety is depictured in green.

Acknowledgements

We gratefully acknowledge Science Foundation Ireland under grant number [19/FFP/6428].

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(P12) Synthetic Magnesium Tetrapyrrole Radicals for Mechanistic Studies of Photosystem II

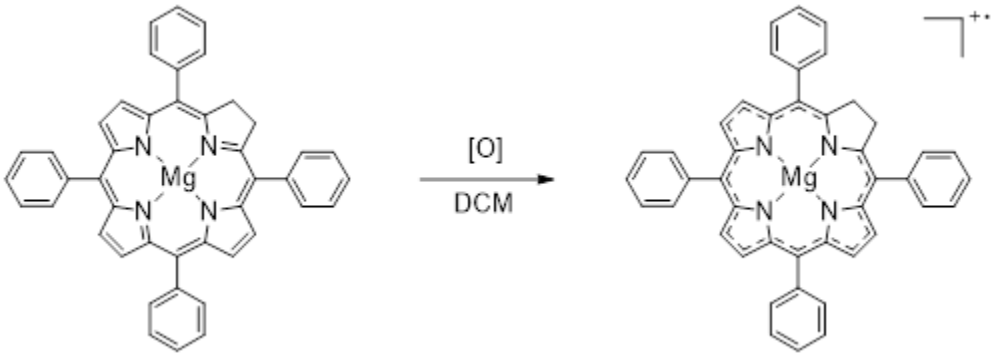
J. M. Thorogood,[a] A. R. McDonald [a]

[a]*Trinity College Dublin, School of Chemistry, Dublin (Ireland); Email: thorogoj@tcd.ie*

Abstract

Magnesium tetrapyrrole derivatives are fundamental to the reactivity of several photosynthetic pigments, most notably the chlorin complex chlorophyll-*a* in P680.[1] The P680 reaction centre consists primarily of 4 chlorophyll-*a* molecules. This gives an overall redox potential of 1.1-1.3 V (vs. SHE) whilst isolated chlorophyll-*a in vitro* has only shown potentials around 0.7-0.8 V.[2] Water oxidation reactions typically require extreme conditions and precious metal catalysts to work,[3] yet photosynthesis occurs under ambient conditions. Taking inspiration from biology, elucidating the conditions and the mechanisms which allow chlorophyll to generate such high redox potentials under mild conditions may lead to ground-breaking improvements in oxidation catalysis.

A series of magnesium porphyrin and chlorin surrogates for chlorophyll-a are synthesised. The oxidation of these to π-cation radicals is carried out via chemical and electrochemical methods. The radical species are then studied by EPR and UV-Vis spectroscopy to optimise the generation of these. After probing the π-cation radicals, their oxidation reactivity towards phenol substrates is investigated via time-resolved UV-Vis spectroscopy. Our promising initial results are presented here including the synthesis of previously uncharacterised π-cation radicals, optimisation of their synthesis and demonstration of their reactivity towards a range of substrates. Ultimately, we aim to develop our findings into a mechanistic understanding of the influence of the tetrapyrrole ligand on natural oxidation chemistry.



Scheme 1. Oxidation of tetraphenylchlorin to its π-cation radical via chemical oxidation.

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(P13) Copper (II) compounds as antimicrobials for the treatment of wound infections.

K. Turzańska,[a] Leila Tabrizi,[b] Mary Pryce, [b] Deirdre Fitzgerald Hughes [a]

[a]Royal College of Surgeons in Ireland/Clinical Microbiology Department, Dublin (Ireland); [b] Dublin City University/ School of Chemical Sciences, Dublin (Ireland)

Abstract

Introduction Antibiotic-resistant bacteria are growing threat to human health, especially in patients with infected wounds and innovative alternatives to antibiotics to treat infected wounds are still being sought. Copper complex compounds are attractive, novel antimicrobial agents for topical use. Naphthalene-Diimide copper complexes (NDI-Cu1) are novel structures with dual antibacterial properties. Here, the antibacterial properties of copper are combined with photoactive antimicrobial properties of NDI. This latter activity is mediated by singlet oxygen produced by light activation, which has a detrimental effect on many bacterial targets. One such complex was investigated here.

Methods In the absence of light, bactericidal activity of NDI-Cu1 was tested against reference strains of each six different antibiotic resistant bacterial pathogens that are the biggest threat to human health (ESKAPE pathognes) by incubating fixed concentrations of each strain with 100 μg/ml in 96-well plates for 24 hours. Photoactivation was investigated by exposing plates to light (420 nm) for 60 min. Hydrogels were prepared with Pluronic F127® incorporating 100 μg/ml of NDI-Cu1 and photoactivation was also measured against selected strains.

Results Without photoactivation, NDI-Cu1 was effective but variable in killing ESKAPE pathogens. The greatest reduction in CFU/ml was found for *S.aureus* ATCC 25923 (6.02 log), *E.coli* ATCC 25922 (5.66 log) and *A. baumannii* ATCC 19606 (5.80 log). NDI-Cu1 had a very good reduction in CFU/ml for *S.aureus* ATCC 25923 (5,93 log) when exposed to a 420 nm lamp for 60 min. When incorporated into a hydrogel, NDI-Cu1 retained bactericidal activity. The NDI-Cu1 compound with Pluronic F127® hydrogel has a very good effect against *S. aureus* ATCC 44330 (5,66 log), *P. aeruginosa* ATCC 27853 (5,99 log) and *A. baumannii* ATCC 19606 (5,19 log) in the dark for 24 hours and in the light condition for 1 hour. NDI-Cu1 was effective in killing biofilms of *S. aureus* ATCC 43300 (42,61%), *S. aureus* ATCC BH1CC (60,37%) and *E.coli* ATCC 25922 (58%) in the dark condition for 24 hours.

Conclusions When developing new and alternative topical antimicrobial agents, the possibility of creating compounds that have dual or targeted antibacterial activity is attractive. Retention of potent activity within a hydrogel was demonstrated here for this novel dual-active photoactive agent. The broad spectrum of activity, included the major AMR pathogens relevant to wound infections. They can be further adapted and modified to achieve targeted, specific and selective antibacterial activity, for advanced applications in infection management.

(P14) The Photophysical Study of DNA Binding Phthalocyanine as Combined Photothermal and Photodynamic Therapeutic Agents

Eleanor R. Windle[a], Christopher C. Rennie[b], Robert M. Edkins[b], and Susan J. Quinn*[a]

[a] *School of Chemistry, University College Dublin, Dublin 4, Ireland*

[b] *Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow, United Kingdom*

eleanor.windle@ucdconnect.ie, susan.quinn@ucd.ie

Abstract

Phthalocyanines are promising photosensitisers for the light-activated anti-cancer therapies: photodynamic therapy (PDT) and photothermal therapy (PTT).[1] They possess advantages over other drugs due to their modifiable photochemical properties, strong absorbance in the biological window and low absorbance at the peak of the solar spectrum but can be hampered by solubility and stereopurity challenges.[2] A library of regioregular pegylated phthalocyanines that are monomeric in DMSO but form soluble aggregates in water have been synthesised.[3] In DMSO, the phthalocyanine is highly emissive which could allow singlet oxygen generation for PDT. In water, there is quenching of luminescence and upon photo-excitation, non-radiative relaxation causes heat release for PTT.

Using UV-vis, emission and CD spectroscopy, the interactions between these phthalocyanines and DNA structures (natural DNA, single-stranded homopolymers, and G-quadruplex structures) were investigated. Upon addition of DNA, the aggregates of complex break apart and large changes are observed in the absorbance and emission spectra. The kinetics and the final aggregation state are affected by buffer concentration, temperature, and the nucleotide:phthalocyanine ratio. This production of monomeric phthalocyanine could shift the cellular death mechanism from PTT to PDT upon interaction with RNA or DNA intracellularly while the kinetics could affect which cell death mechanism dominates over time.

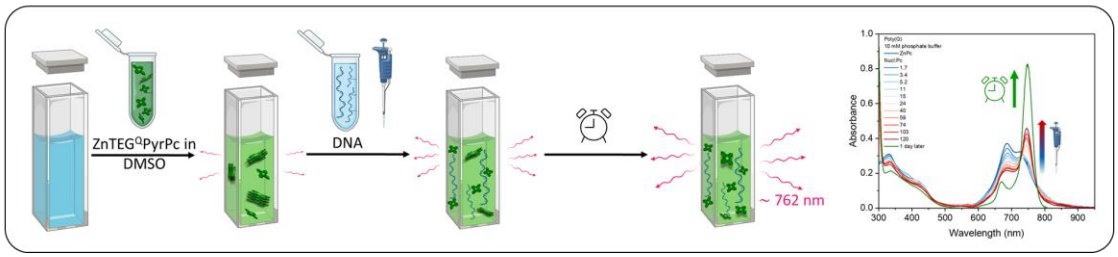

Figure 1: Schematic of addition of DNA to phthalocyanine stock and change in UV-vis spectrum upon addition of poly(G) and following 24 hours.

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(P15) The Lanthanide Detective: The Hunt for Unlabelled Lectins and Antiadhesive Antimicrobials

K. Wojtczak[a], I.J. Murphy[a], Kevin Kavanagh[b], J.P. Byrne[a,b]

[a]University of Galway, School of Biological and Chemical Sciences, Galway (Ireland); [b]Maynooth University, Department of Biology, Maynooth (Ireland); [c]University College Dublin, School of Chemistry, Dublin (Ireland); k.wojtczak1@universityofgalway.ie

Abstract

Lanthanide probes are advantageous for sensing applications due to their characteristic and time-resolved emission spectra, which can be easily distinguished from background fluorescence of biological samples.[1] Many pathogenic bacteria such as *Pseudomonas aeruginosa* (PA) produce lectins which present viable targets for detection, as well as for new therapies. Diagnostic methods for bacterial infections rely on cell culture, leading to delays in targeted treatment. New detection methods are needed in the fight against antimicrobial resistance. This project aims to use the selective nature of carbohydrate-lectin interactions to develop visually responsive glycoconjugate probes, which would be suitable for diagnosis of infections, such as by PA, a bacterium classified as a Priority 1 pathogen by the WHO. LecA and LecB are lectins on the surface of PA with high affinity for galactoside and fucoside glycans respectively.[2] Many approaches have been developed to inhibit the binding of these lectins to human tissue cells by the development of inhibitory glycoconjugates with varying degrees of success.[3] Here we report two generations of multivalent glycoconjugate lanthanide complexes, featuring different architectures, which demonstrate enhanced emission in the presence of relevant lectins as divalent and tetravalent systems.[4] Integration of these systems into smart materials has potential for application in the medical devices industry. We also present a series of transition-metal glycoconjugates which have been tested for biological activity against PA and *Candida albicans*.

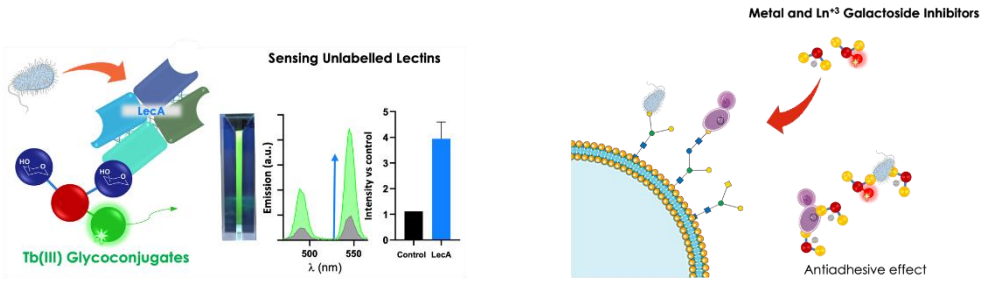

Figure 1. Graphical abstract.

Acknowledgements

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(P16) Spectroscopic study and DNA binding of luminescent carbon dots

C. Zehe,[a] D. Kriszan,[a] S. J. Quinn[a]

[a]*University College Dublin, School of Chemistry, Dublin (Ireland); clara.zehe@ucdconnect.ie*

Abstract

Carbon dots (CDs) have emerged as an exciting group of materials since their discovery in 2004[1] due to their luminescent properties, small size and low toxicity.[2] However their luminescence mechanism is still subject to debate.[3] The optical response of many CDs is sensitive to their environment, which has been applied for chemical, biological cell and bacteria sensing.[2, 4] This work highlights the photophysical properties of yellow luminescent CDs and demonstrates their binding and luminescent response to DNA.

CDs of size 3.1 ± 1.8 nm were prepared from o-phenylenediamine (oPD) via a solvothermal method.[5] The CDs absorb in the visible at 420 nm and show bright luminescence with a maximum at 570 nm and a PLQY of 13.6% in ethanol. Their luminescence showed a bathochromic shift from 522 nm in the aprotic solvent DMSO to 570 nm in water, accompanied by a reduction in emission intensity. Good emission is observed in alkaline and neutral solution, which is lost under acidic conditions (< pH 5). In presence of DNA, luminescent quenching and spectroscopic shifts of absorbance and emission maxima are observed. Particularly strong optical response is seen in the presence of guanine-rich DNA systems with strong quenching observed. Ultrafast spectroscopy resolved surface state contribution to their luminescence. The extent of luminescent quenching and optical shifts when CDs interact with their environment could be promising tools for biological sensing.

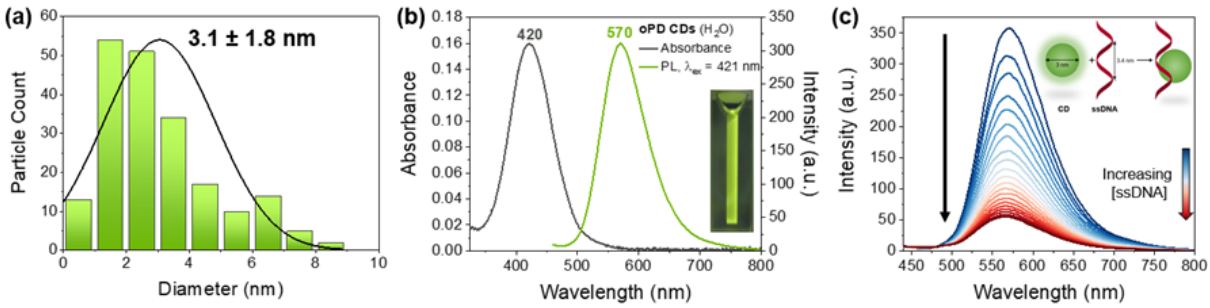

Figure 1. (a) Size distribution of CDs from AFM topography on a mica substrate, **(b)** absorbance and photoluminescence spectra of yellow luminescent CDs and **(c)** increasing luminescence quenching in the presence of single stranded DNA showing a schematic of the interaction and quenching process.

Acknowledgements

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