Durham University

Engineering and Physical Sciences Research Council

Newcastle University

MoSMed CDT Newsletter

ISSUE 03

February 2021

MoSMed Molecular Sciences for Medicine

Notes from the Editors

Happy belated New Year and welcome to the first MoSMed CDT Newsletter of 2021! Since our last issue, MoSMed held its 2nd Annual Conference virtually in December, which was a great success with approximately 78 participants joining in from around the world each day. The Conference is a highlight in our annual CDT calendar showcasing our research and bringing together our doctoral researchers, academic colleagues and external partners in an open dialogue to discuss all the exciting research taking place at the forefront of molecular and medical sciences! During such sombre and difficult times with the ongoing pandemic, it was a nice opportunity to come together and be a part of something special. We are also excited to announce that recruitment for our next cohort of Doctoral Researchers is now OPEN! Details are available on the MoSMed website. We hope you enjoy reading this issue of our newsletter. Wishing everyone a safe, healthy and productive start to the year!

Abbey Butler, Olivia Gittins, Selina McCarthy and Emma Worden

In this issue.

New MoSMed Blogs!

Follow the progress of Cohort 1 students' projects in their blogs to be found on our website here: https://research.ncl.ac.uk/mosmed/impact/blogs/

The 2nd MoSMed Annual Conference: Dec 2020.

By Emma Worden (MoSMed CDT Manager - Durham)

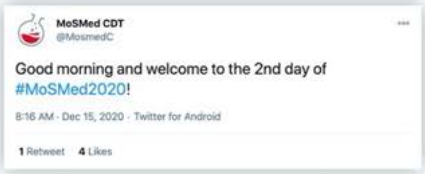
The 2nd MoSMed Annual Conference was scheduled to be delivered in Durham this time, however like many events in the last year, its delivery online was dictated by the situation related to COVID-19. The Conference was held over three days (14th,15th and 16th December with one day of pre-recorded content and two days of live events delivered over Zoom). One of the highlights of the event were the presentations by both our cohorts of gifted Doctoral Researchers. In the face of adversity this year, our students have shown great resilience in determinedly persevering with their research and developing their knowledge of their subject whilst expanding their skillset.

Both of our cohorts contributed directly to our Conference to share their research projects. Our Cohort 1 Doctoral Researchers designed and presented an academic poster, with the further opportunity of hosting a Question-and-Answer session based on this. Our Cohort 2 Doctoral Researchers, who only commenced their PhD studies in September 2020, rose to the challenge of starting a PhD in the midst of a global pandemic and further demonstrated their resilience and talent by giving three-minute presentations outlining their research projects at the Conference.

It was a testament to all our students' brilliance and commitment that resulted in the delivery of truly confident and impressive presentations, which captured the progress made so far and highlighted their future plans related to their research projects. These presentations deservedly received universal praise from our academic colleagues and industry partners. We awarded prizes for the top presentations and posters as voted by the Conference participants and CDT Management teams and we are extremely grateful to Arcinova, Astex and Almac who kindly agreed to sponsor the prizes. Details of our four amazing prize winners can be found under the 'News' section of this newsletter and the MoSMed CDT website. We were fortunate enough to host a range of fantastic national and international speakers at our event, including Carrie Ambler (Durham University/ LightOx), Simon Croft (DNDI), Gareth Jenkins (Arcinova), Lynn Kamerlin (Uppsala University), Christoph Mueller-Dieckmann (ESRF), Martin Walsh (Diamond) and Francesca Stanzione (CCDC). All sessions were expertly chaired by some of our Doctoral Researchers.

Shahidur Chokdar *(UKRI EPSRC): "It was great to see such a well-run conference with confident students from both Cohort 1 and Cohort 2 delivering coherent presentations. The guest speakers certainly added value and shall provide good food for thought for future discussions."*

Tweets from **Catherine Salvini**, one of our **aligned Cohort 1 Doctoral Researchers**, capturing the main events and highlights of our Conference.



Attendees were also involved in the discussion and development of potential future projects related to the CDT's three main themes: Biology of Disease (led by Paul Denny); Structural Biology and Computation (led by Agnieszka Bronowska); and Molecule and Assay Design (led by Matthias Trost). Overall, this year's online conference was deemed a success by all! Here are some thoughts from a few of our attendees:

Malcolm Walkinshaw *(Wellcome Trust Centre for Cell Biology (WTCCB) and MoSMed CDT Advisory Board member)*:
"I very much enjoyed the two-day MoSMed CDT Annual Conference in December and was most impressed at the high quality of all of the presentations. It is truly remarkable that, despite the COVID restrictions, everyone has been so productive and managed to generate so much interesting science."

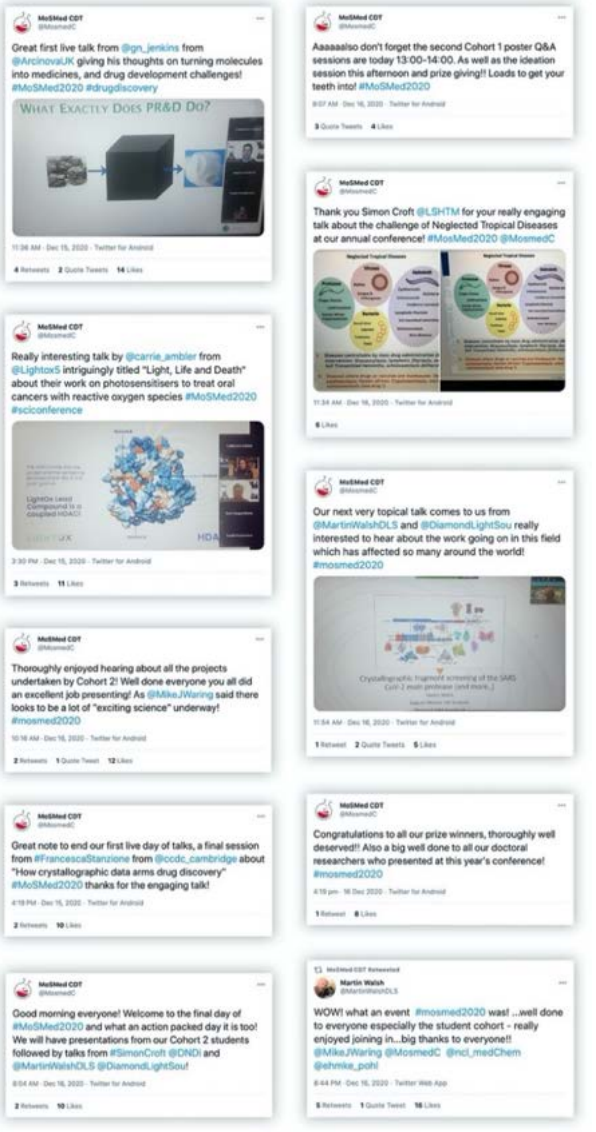
Christoph Mueller-Diekmann *(Deputy Head of the Structural Biology group at the ESRF in Grenoble, France):*
"This was an extremely well organised virtual conference, I really enjoyed meeting the students and having the opportunity to talk to them in the various sessions. I was particularly impressed by the quality of their presentations—you have got an extraordinary group of students."

David Hollinshead *(Technical Director, Elixir Software Ltd and MoSMed Advisory Board Member)*:
"I was extremely impressed by what has been achieved despite adversity, and the commitment and collaboration demonstrated across the institutes and all the players. So, my thanks are expressed to all involved in the CDT initiative and I wish them well for the realisation of the next phase of their endeavours."

Jessica Graham *(Second-year MoSMed Doctoral Researcher)*:
"What a fabulous few days at the MoSMed Annual Conference 2020. It was great to hear the exciting research that my peers have been carrying out and it was truly inspirational to hear from a diverse set of guest speakers. Can't wait for next year!"

We remain hopeful (fingers and toes crossed!) that our next Conference, scheduled for December 2021, will be delivered in-person and we look forward to being able to share our updates and research progress with all of our valued partners, colleagues and Doctoral Researchers against the beautiful backdrop of Durham University. For now, please stay safe and we will see you soon!

Prof. Mike Waring *(MoSMed CDT Director):*
"*The 2020 MoSMed Annual Conference was a great opportunity to formally welcome our 2nd cohort and for everyone to hear about their project plans, as well as to hear about the progress that our first cohort have made this year. It was not the same as a face-to-face meeting but the event was fantastically well organised and ran very smoothly, thanks to the efforts of Trudi and Emma with our student representatives. It was really nice to see so many of our partners join the meeting and to engage so proactively with the events. The presentations highlighted how well everyone has coped with the trials and tribulations of COVID in 2020, both in terms of still making progress and with presenting work in the virtual world. At the end of the event, some students were singled out as worthy prize winners, well done to them, but everyone did really well.****"***



Introducing our new Cohort 2 Doctoral Researchers.

A Virtual Welcome! Induction session for our newest cohort in October 2020.

Meet the new Cohort!

Siddique Amin – MRes in Chemistry (University of Glasgow)

Matt Anderson – BA & MSci (Integrated Masters) in Natural Sciences (University of Cambridge)

Arron Bale – Masters in Mathematics (Durham University)

Abbey Butler – Masters in Biochemistry (University of St Andrews)

Ben Cree – Masters in Chemistry (Durham University)

Katie Dowell – Masters in Chemistry (University of Reading)

Allen Drews – Masters in Scientific Computing and Data Analysis (Durham University)

Katie Gristwood – Masters in Biological Sciences (University of Liverpool)

Dorota (Dori) Gasparikova – Masters in Chemistry (University of Warwick)

A few words from Dori Gasparikova about starting her PhD: *"Participating in the Foundations of Science course this year was very enjoyable and useful. In particular, I enjoyed presenting and hearing about different cases of fraud in science, mainly because it reminded me of the importance of critically assessing papers and information I might be reading and researching."*

In a year like no other, we were delighted to welcome our new cohort of Doctoral Researchers! Despite restrictions preventing us meeting in person, we were determined to think creatively to offer online alternatives to an in-person induction to MoSMed and to deliver the usual training opportunities.

We welcomed Cohort 2 to the MoSMed community by recreating our induction event online, including an Escape Room social event for both the new and existing students, supervisors, and members of the management team. This has since become a much talked about and memorable event within the MoSMed community! Our new cohort have found opportunities to get to know each other and have managed to fully engage with the online version of the first year 'Foundations of Science' course (led by our Durham Lead Ehmke Pohl). This included some interesting discussions around the definition of Science, the Philosophy of Science and culminated in some impressive presentations on the subject of scientific fraud cases. Further modules related to this course that have been delivered online, including 'An introduction to Python' (Matteo Degiacomi – Durham University) as part of the 'Computational Matters' module and 'ED&I Matters' (Michelle Taylor – Durham University).

In addition, both cohorts have benefitted from online seminars from both our academic supervisors and the wider MoSMed community. In preparation for the conference, specific training on producing academic posters, delivering effective presentations and online networking was delivered by Dr Pete Whitton at the Durham Centre for Academic Development. Further training included 'Time Management' (Eleanor Loughlin – Durham University) and 'LaTeX for Beginners' (Halim Kusumaatmaja – Durham University). We are excited to offer another term of varied training and seminar programmes, despite the continued restrictions, and particularly look forward to the first of our cohort-led seminars to be delivered by Ruth Walker and Olivia Gittins.

We have all been truly impressed by the resilience and enthusiastic engagement shown by our first-year Doctoral Researchers in having integrated into our community. Furthermore, through a buddying scheme, our second-year Doctoral Researchers have been instrumental in offering advice and support to our new starters, which has in turn helped them to settle into the first few months of their PhD.

One of the members of the new cohort, Siddique Amin has provided

Meet the new Cohort!

Lydia Hallam – MChem with Honours in Chemistry with Medicinal Chemistry with Study Abroad (Newcastle University)

Dominic Harrison – Masters in Physics (Newcastle University)

Sam Hogan – BSc in Biological Sciences (University of East Anglia)

Leonie Müller – Master of Science (University of Bremen)

Robyn Poulton – Masters in Chemistry (Heriot-Watt University)

Filomena Saulino – MSci in Pharmaceutical Chemistry and Technology (The University of Salerno)

Helen Sims – MSc in Engineering (University of Cambridge)

Chantal Stenger – Masters in Science (University of Zurich, then work in industry)

Kenneth Zhi Jian Tan – Master of Research (Cancer) (Newcastle University)

Find out more about Cohort 2 on their website profiles here: https://research.ncl.ac.uk/mosmed/people/students/cohort22020-present

We are recruiting for September 2021!

MoSMed are currently recruiting for its third cohort of Doctoral Researchers to commence their studies in September 2021. We have a range of exciting projects including co-funded opportunities with some of our industrial partners. Information about studentship opportunities and how to apply can be found on the MoSMed website at: https://research.ncl.ac.uk/mosmed/phdstudentships. For all application enquiries, please contact: mosmed.cdt@ncl.ac.uk

an account of what it has been like to start a PhD with MoSMed in the midst of a global pandemic which, as we look to recruit another cohort of talented researchers, we thought is a particularly relevant insight at this time.

"Starting my PhD during a pandemic has been quite the rollercoaster. When moving to a new city, my first instinct would be to go out and explore all of the sites, try out the local restaurants and meet new people. Lockdown has prevented me from doing most of these things, so finding a sense of belonging was particularly challenging. Things got better when the MoSMed inductions began and I was able to 'meet' everyone. We had lots of ice-breaker sessions where we got to learn about each other's projects and share fun facts about ourselves. A particular highlight was a virtual Escape Room, where we were put into teams to work together to solve puzzles to track down a suspect for MI5—not to brag too much but my team came first, albeit after bending the rules just a little. Since then, we've organised other social events such as virtual quizzes and a Christmas social, which have helped bring us together as a cohort."

Siddique also added that there are many opportunities to get involved in within the MoSMed CDT: *"The CDT is also shaped by student engagement and feedback. As such, there are student representatives for each cohort with roles including Cohort Chair and Deputy Chair, as well as Outreach, Social and Newsletter Representatives amongst others. My role as Cohort Chair consists of engaging with my cohort to gather their feedback and liaising with the CDT's Executive Committee to ensure that the opinions of the cohort are fairly represented."*

Finally, when asked to sum up how he has found making progress on his PhD studies in these first few months, Siddique said: *"As my project is lab-based, I was delighted to learn that I could still conduct my work in the lab despite lockdown; however, adapting to all of the COVID measures definitely took some getting used to. To adhere to occupancy limits and social distancing guidelines, I have to book my time in advance, which requires some planning and coordination with the other lab members. Being supervised and shown new techniques has felt like an interpretive dance at times; however, after a few weeks of adapting it no longer feels like a big hinderance. As a matter of fact, the restrictions have helped me learn how to better plan my work and maximise my efficiency in the lab. I admit that I was apprehensive and nervous about moving to a new city and beginning my PhD during such a tough and isolating time, but being part of a CDT with people who are in the same boat as me has made me feel far less alone. The combination of all of the MoSMed events, and having such a supportive lab group, has helped me gain the sense of belonging that I feared I would lack prior to starting my PhD."*

MoSMed Industrial Partners: Diamond Light Source.

By Olivia Gittins (Cohort 1)

Synchrotrons generate extremely powerful X-rays by accelerating electrons in a ring to near the speed of light, producing beams of light ten billion times brighter than the sun. This light is used to study a wide variety of samples from fossils to viruses, with the beams of light produced by the synchrotron directed off into various 'beamlines' with specialised areas of study.

In this issue of the MoSMed newsletter, I found out more about another of our industrial partners, Diamond Light Source. As the UK's national synchrotron facility around 14,000 researchers from academia and industry, spanning a range of research areas, use Diamond to conduct experiments. Diamond is a not-for-profit organisation which is jointly funded by UK Research and Innovation (UKRI) and Wellcome Trust. As such, facilities including the synchrotron and cryo-electron microscopy are available to researchers for free through a competitive application process, subject to the publication of results in the public domain.

As a world-leading centre for synchrotron science, Diamond helps drive scientific discovery and innovation in both academic and industrial settings across the UK. One particularly topical example of such research excellence is the fantastic 'COVID MoonShot' project, which was initiated in response to the COVID-19 pandemic.

During the 2nd Annual MoSMed Conference (December 2020), Dr Martin Walsh from Diamond gave an excellent talk covering the crystallographic fragment screening of the SARS-CoV-2 main protease (MPro), which took place on the I04-1 beamline at Diamond. The team were able to solve a new structure of MPro at high resolution (PDB ID: 6YB7) and determine that the active site was empty and solvent accessible—perfect for fragment screening. The data generated from the fragment screen was then assessed through a fully open initiative: the COVID MoonShot.

See the research paper about this work here: https://doi.org/10.1101/2020.05.27.118117

Dr Alice Douangamath is the Senior Beamline Scientist responsible for the XChem (X-ray structure-accelerated, synthesis-aligned fragment medicinal chemistry) facility and its academic user program. Having contributed to the construction of the I04-1 beamline and the development of the XChem platform, Alice's work is integral to the success of fragment screening campaigns which take place at Diamond, such as the MPro fragment screen. At the I04-1 beamline, the full X-ray screening experiment has now been implemented as a highly streamlined process, allowing up to 1000 compounds to be screened individually in less than a week (including 36 hours of unattended beamtime). Alice has kindly agreed to tell me a bit more about her work:

How did your research background lead you to work at Diamond?

"I am a physicist by training and did my PhD in a synchrotron in Hamburg and I have always enjoyed the synchrotron atmosphere (a mix of high tech and friendly, crazy/nerdy scientists who could spend entire nights conducting pretty cool experiments!). After my PhD, I went into drug discovery in industry because I was convinced (and still am) that structural biology can play an important role in that field. When I was offered to help build a beamline, for which the main purpose would be high-throughput ligand binding studies, I guess that's when everything just came together."

What are some highlights from your career at Diamond so far?

"Getting I04-1 built and operational was a huge relief! Jose Brandao-Neto and I had worked really hard with the group of support team to have it working! Of course, XChem is pretty successful and being able to show the resilience of this team and platform through our COVID work in a very hard time is something we can be proud of as a group."

Did you encounter any challenges in carrying out the SARS-CoV-2 MPro crystallographic fragment screen?

"The hardest was to combine working under extremely pressing conditions to obtain the data before the shutdown and the first lockdown, and then analyse the data to get them released rapidly whilst finding my way around living in lockdown and home-schooling. Basically, all of the problems working carers have encountered (and are still encountering…). I am grateful to my family for their understanding and support through those months! I also want to say that I am very privileged to work in a great, fun and so efficient team!"

I also wanted to know more about working with Diamond as an academic user. MoSMed's very own Prof. Ehmke Pohl has a wealth of experience in carrying out experiments at Diamond and was happy to share his experience as a Diamond user:

What type of experiments does your group carry out at Diamond and on which Beamlines?

"Our groups in Durham (mine and Tim Blower's) use all of the macromolecular crystallography beamlines, I03, I04 and I04-1. However, my favourite beam line is I24, the microfocus beam line. It is at least one-order of magnitude brighter than the others. Automation and remote control now work very reliably on all beamlines and we have not been on-site at Diamond for over a year. For us, the most exciting development is the VMXm beamline, which will combine X-ray diffraction with electron microscopy, providing a sub-µm focused X-ray beam. In addition, we use the I22 beamline for BioSAXS when crystals cannot be obtained or to look at large conformational changes upon binding events."

How do you set up experiments at Diamond?

"Access to all Diamond beamlines is provided via our Block Allocation Group (BAG) allocation shared between Newcastle, Durham and York, which is organised by Jahn Turkenberg (York), Arnaud Basle (Newcastle) and Ehmke Pohl (Durham). So, simply speak to your supervisor and contact Arnaud or Ehmke. They may also offer advice on crystallisation if you want to use the MX beamlines (and they are generally reasonably friendly). As Diamond is a MoSMed partner, there is the option for placements (post-pandemic!)—ideally as part of a collaboration. The facilities include the Membrane Protein Laboratory (MPL), a crystallisation facility, the fragment screening facility (XChem) and the XFEL hub, which provides a link to the X-ray Free Electron Laser in Hamburg. If you are interested in any of these, but you or your supervisor does not yet have contacts, talk to Ehmke or Mike and we will help!"

Arron Bale from Cohort 2 is working on 'Developing reliable *ab-initio* software for the interpretation of protein structure from BioSAXS data' and is partly funded by Diamond.

I asked Arron if he could share how his work benefits from his partnership with Diamond, as well as the sort of experiments that he will be carrying out in collaboration with them: *"A novel ab-initio method for protein structure determination from BioSAXS data was pioneered by Prof. Chris Prior, using a discrete differential geometry (DDG) approach. (See the research paper about this work: https://pubs.acs.org/doi/10.1021/acs.jctc.9b01010). My project seeks to develop this method and implement it at the high-throughput BioSAXS beamline (B21) at Diamond. Alongside the use of this dedicated state-of-the-art beamline, I am also fortunate to benefit from the expertise of Robert Rambo, Science Group Leader for the Soft Condensed Matter Village. Structural information from crystallography or electron microscopy (EM) can be useful for testing the effectiveness of this method, so the broad portfolio of synchrotron and cryo-EM techniques on-site will be hugely beneficial for me. My future aims include producing an online web service and training materials for this DDG modelling approach, which will be implemented on the B21 beamline."*

In setting out to learn more about Diamond, I have gained a sense of the widescale impact of their work throughout the scientific community, both nationally and internationally. Scientists from all manner of disciplines have benefitted from research conducted at Diamond Light Source and there will no doubt be some fantastic work carried out by our MoSMed students, in partnership with Diamond, as the CDT grows and progresses.

You can find more information about the research facilities and activities taking place at Diamond Light Source on their website: https://www.diamond.ac.uk/Home.html

You can also find out more about Arron's research project, as well as the work of other MoSMed Students on the MoSMed website: https://research.ncl.ac.uk/mosmed/people/students/

2020 and the impact of COVID-19 summed up in 15 tweets.

By Steven Cobb (Professor of Chemical-Biology – Durham and MoSMed CDT Training Programme Lead) (@Cobb_Group)

"This pretty much sums up my year as an academic and a dad in 2020"

January

March

May

June

MoSMed Molecular Sciences for Medicine

September

The Cobb Group
@Cobb_Group

School starts again tomorrow and at 6pm our son let us know he has out grown all of his trousers. Similar feeling as to going to submit a grant and realising you only have 30 mins to write the GANTT chart #Lastminuterush #frantic #ontheclock

8:12 PM · Sep 2, 2020 · Twitter for Android

21 Likes

The Cobb Group
@Cobb_Group

Just had my sons complain that I was "too noisy and disruptive" while they were on a Zoom call playing Fornite with their friends 😂😂🤣😂😇.....

5:20 PM · Sep 19, 2020 · Twitter for Android

11 Likes

The Cobb Group
@Cobb_Group

I am very fortunate to have two fantastic #postdocs in the group. Both outstanding scientists, with very bright futures ahead of them. Thank you Diana @DGimenez_ibanez and Will @WDGBChem for all you do for the @Cobb_Group 👏👏👏👏 #NPAW2020 #awesomepostdocs

7:43 AM · Sep 26, 2020 · Twitter for Android

1 Retweet 7 Likes

The Cobb Group
@Cobb_Group

Running a 50% occupancy COVID-19 safe lab, a new teaching year starting with "blended learning", self-isolating kids bring second round of home schooling and dodgy internet makes academia currently feel like a giant and never ending game of whack-a-mole 😵 #isit2021yet

6:15 PM · Sep 30, 2020 · Twitter for Android

13 Likes

October

The Cobb Group
@Cobb_Group

The fantastic Ron Zuckermann @molecularfndry kicking off the new online #peptoid Symposia really looking forward to this talk #peptoidsymposium @Durham_BSI

3:39 PM · Oct 27, 2020 · Twitter for Android

1 Retweet 6 Likes

November

The Cobb Group
@Cobb_Group

Dreaded Friday night email received informing us that another case of COVID in our kid's school is putting us back into isolation and home schooling again. At least my high school math skills are improving in this pandemic. Anyone have a geometry problem that needs solving?

7:18 PM · Nov 13, 2020 · Twitter for Android

12 Likes

Pinned Tweet

The Cobb Group
@Cobb_Group

Will need to remember how to change my email signature properly but for tonight this will do. Huge thanks to all Cobb family members, @Cobb_Group researchers past and present, and long term collaborators. I owe each of you a beer, malbec, whisky, iron bru.. . Cheers 🥂👍😎

Steven L Cobb

~~Associate~~ Professor of Chemical-Biology

Director of the Biophysical Sciences Institute (Durham)
Deputy Coordinator of the GCRF/ MRC Network for Neglected Tropical Diseases (https://ntd-network.org/)

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Send Discard

9:25 PM · Oct 29, 2020 · Twitter for Android

1 Retweet 3 Quote Tweets 150 Likes

December

The Cobb Group
@Cobb_Group

Day two of the @MosmedC CDT conference #MosMed2020 great presentation by @Cobb_Group new PhD student Katie - well done 👏👏

9:38 AM · Dec 16, 2020 · Twitter for Android

2 Retweets 1 Quote Tweet 17 Likes

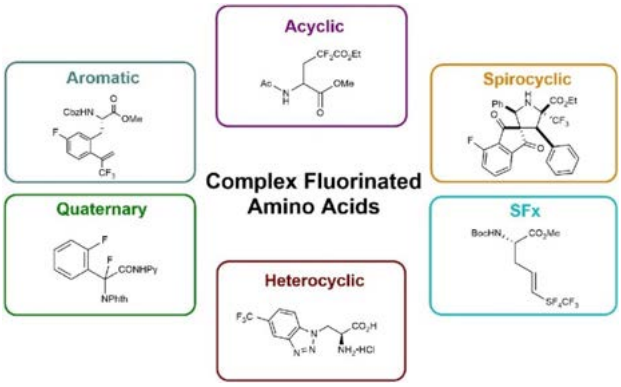
MoSMed Molecular Sciences for Medicine

Recent Publications.

Synthesis of complex unnatural fluorine-containing amino acids

William D.G. Brittain, Carissa M. Lloyd, Steven L. Cobb, 2020, Journal of Fluorine Chemistry, Volume 239;
https://doi.org/10.1016/j.jfluchem.2020.109630

"The area of fluorinated amino acid synthesis has seen rapid growth over the past decade. As reports of singly fluorinated natural amino acid derivatives have grown, researchers have turned their attention to develop methodology to access complex proteinogenic examples. A variety of reaction conditions have been employed in this area, exploiting new advances in the wider synthetic community such as photocatalysis and palladium cross-coupling. In addition, novel fluorinated functional groups have also been incorporated into amino acids, with SFX and perfluoro moieties now appearing with more frequency in the literature. This review focuses on synthetic methodology for accessing complex non-proteinogenic amino acids, along with amino acids containing multiple fluorine atoms such as CF3, SF5 and perfluoroaromatic groups."



Current Synthetic Routes to Peptidyl Mono-Fluoromethyl Ketones (FMKs) and Their Applications (Review)

Carissa M. Lloyd, Neil Colgin, Steven L. Cobb, 2020, Molecules 2020, 25(23), 5601; https://doi.org/10.3390/molecules25235601

"Peptidyl mono-fluoromethyl ketones (FMKs) are a class of biologically active molecules that show potential as both protease inhibitors for the treatment of a range of diseases and as chemical probes for the interrogation of cellular processes. This review describes the current solid- and solution-phase routes employed for the synthesis of peptidyl mono-FMKs. In addition, it provides a brief overview of some of the key applications of FMKs in the fields of chemical biology and medicinal chemistry."

Molecular basis for substrate specificity of the Phactr1/PP1 phosphatase holoenzyme

RO Fedoryshchak, M Přechová, Abbey M Butler et al., 2020, eLife, 9:e61509; https://doi.org/10.7554/eLife.61509

"PPP-family phosphatases such as PP1 have little intrinsic specificity. Cofactors can target PP1 to substrates or subcellular locations, but it remains unclear how they might confer sequence-specificity on PP1. The cytoskeletal regulator Phactr1 is a neuronally enriched PP1 cofactor that is controlled by G-actin. Structural analysis showed that Phactr1 binding remodels PP1's hydrophobic groove, creating a new composite surface adjacent to the catalytic site. Using phosphoproteomics, we identified mouse fibroblast and neuronal Phactr1/PP1 substrates, which include cytoskeletal components and regulators. We determined high-resolution structures of Phactr1/PP1 bound to the dephosphorylated forms of its substrates IRSp53 and spectrin αII. Inversion of the phosphate in these holoenzyme-product complexes supports the proposed PPP-family catalytic mechanism. Substrate sequences C-terminal to the dephosphorylation site make intimate contacts with the composite Phactr1/PP1 surface, which are required for efficient dephosphorylation. Sequence specificity explains why Phactr1/PP1 exhibits orders-of-magnitude enhanced reactivity towards its substrates, compared to apo-PP1 or other PP1 holoenzymes."

If you have any recently submitted journal articles or reviews that you would like to be included in the next newsletter issue, please email mosmed.cdt@newcastle.ac.uk

Caption Competition.

Caption this image! *What do you think they are talking about?*

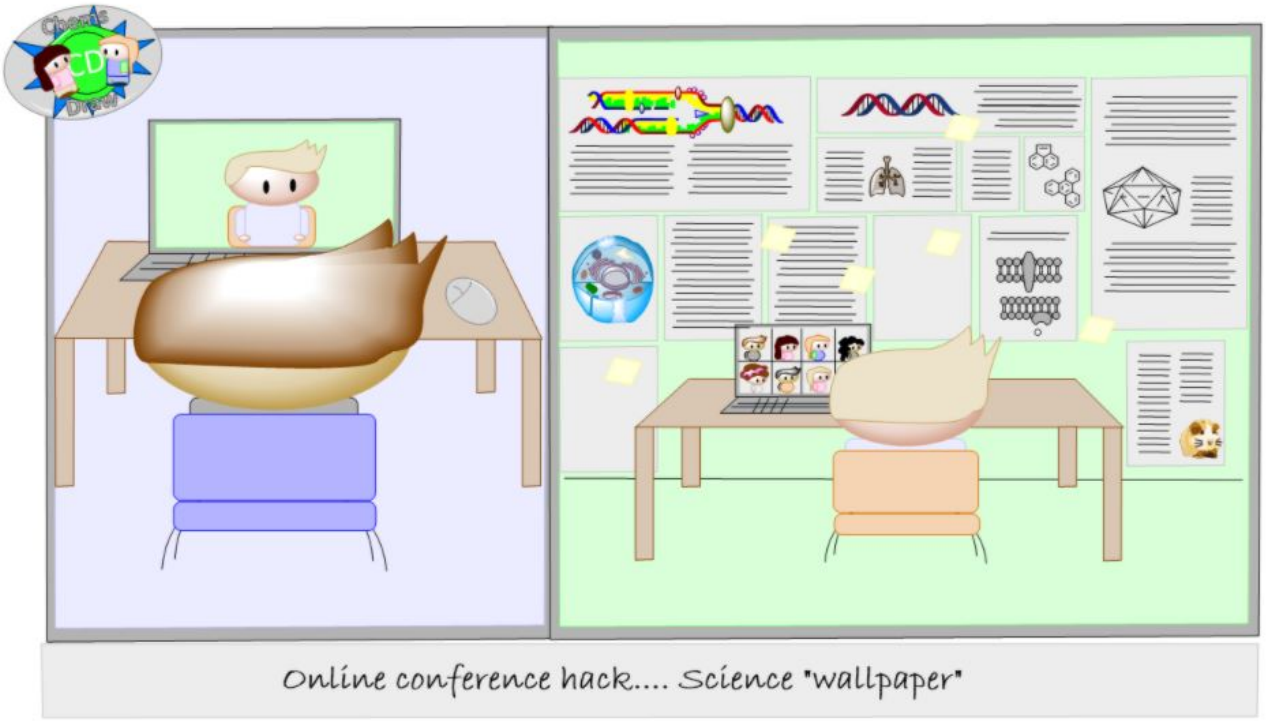
February 2020: This was a great day (pre-COVID restrictions) with Prof. Jim Naismith, Director of the Rosalind Franklin Institute who visited the Chemistry Department at Durham University to deliver his RSC Tilden Award Lecture and talk to our MoSMed Doctoral Researchers about the work of the new Rosalind Franklin Institute located at the Harwell Science and Innovation Campus in Oxford (@RosFrankInst).

Photo credit: Ehmke Pohl, with thanks to Jim Naismith and the MoSMed Doctoral Researchers.

Please submit your best humorous/witty/silly captions to mosmed.cdt@newcastle.ac.uk by 26th February. The winning caption will be chosen by our MoSMed CDT Managers Selina McCarthy and Emma Worden, and a yummy prize will follow!

Chemistry Cartoon.

Created by the very talented Catherine Salvini and Isaline Castan of Cohort 1 using ChemDraw!



News and Updates

Congratulations

Congratulations to four members of our MoSMed community on their promotions to Professor. These include our brilliant Durham CDT Lead and MoSMed Co-Director Ehmke Pohl; our fantastic PIs Steven Cobb and AnnMarie O'Donoghue; as well as Jacquie Robson, a valued member of our MoSMed Management Board. Well done to all on this great achievement!

Congratulations also to four of our Doctoral Researchers who won prizes at our MoSMed Annual Conference and thank you to our sponsors for kindly donating the prizes:

- Best Poster (Cohort 1) as voted for by the MoSMed Strategic Advisory Board, sponsored by Astex – Isaline Castan for her poster entitled: *'Expanding the scope of S_NAr for DNA-Encoded Library Synthesis'.*
- Best Poster (Cohort 1) as voted for by the Conference attendees, sponsored by Arcinova – Rachael Pirie for her poster entitled: *'Evaluating 3D Shape-Similarity For Drug Discovery'.*
- Best Presentation (Cohort 2) as voted for by the MoSMed Executive Committee, sponsored by Almac – Abbey Butler with *'Unravelling the mysteries of retinoid signalling'* and Lydia Hallam with *'Small molecule tools to target glucose metabolism in Non-Alcoholic Fatty Liver Disease (NAFLD)'.*

Hello and Goodbye!

In December, we were delighted to welcome back Selina, our CDT Manager at Newcastle, from maternity leave. Selina was straight back into the swing of things with last-minute Conference preparations, and a MoSMed Christmas (virtual) social to look forward to! Trudi, who was providing maternity cover for Selina, also left us in December.

Trudi wanted to express her appreciation to everybody involved with MoSMed for making the last nine months a very enjoyable experience:

"Thank you so much to the MoSMed team, as starting (and finishing) a job during a global pandemic has definitely been different, and although I didn't get to meet anybody in person, you have made me feel welcome and a part of the team. I'd especially like to mention the MoSMed Doctoral Researchers who have impressed me throughout with their determination, enthusiasm and kindness. I have no doubt that you all have a very bright future ahead of you, and I look forward to hearing about all of your successes. Take care of yourselves, and each other."

Thank you

I would also like to welcome our newest member of the newsletter editing team, Abbey from Cohort 2! She has brought some fantastic design skills and artistic flair to the newsletter, which I'm sure you'll agree is looking great.

Upcoming Events

- Dates for your diary: **15-16th December 2021: 3rd Annual MoSMed Conference**. Join us later this year for the 3rd MoSMed Annual Conference. Details about our recent Conference in December 2020 can be found on the MoSMed website.
- MoSMed is recruiting! PhD Studentships are now available to start in September 2021. Keep checking the MoSMed website for more details.
- High Force Research are celebrating International Women and Science Day on 11th February 2021 through their 'North East Women in Chemistry' event! See their website for details.
- The Bionow Life Sciences Careers Fair: 17-18th March 2021. Bionow is a non-profit membership organisation supporting the life sciences/biomedical sector across Northern England. Find out more here.
- Get in touch! We love to hear from all of our MoSMed community – if you have any upcoming events or information that you would like to share, please email mosmed.cdt@newcastle.ac.uk or tweet us @MosmedC.

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Feedback and suggestions are always welcome.
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