

Marina Demetriades, PhD, BSc



ACADEMIC POSITIONS

- Oct 2014-Present **Postdoctoral Research Associate, Department of Biochemistry, University of Oxford**
Project: Phosphoprotein Phosphatases in Cell cycle regulation- New cancer targets
Developed and applied novel methods to modify peptides and to chemically modify proteins. Synthesised macromolecular peptidic-based affinity probes
Culture of mammalian (Hela, HEK 293) and insect cells (SF9, High 5) for protein production
Supervised by Prof Francis A. Barr
- Nov 2013- Sep 2014 **Postdoctoral Research Assistant, Department of Chemistry, University of Oxford**
Project: Inhibition and mechanistic studies on DNA and RNA demethylases
Developed a novel *in vitro* enzyme activity assay (fluorescence, MALDI-TOF MS, LC-MS)
Optimised crystallisation methods and used crystallographic analyses for inhibitor design
Supervised by Prof Christopher J. Schofield
- Sep 2011- June 12 **Invigilator for College and University examinations, University of Oxford, UK.**
- Jan-Mar 2011-13 **Junior Laboratory Demonstrator, Department of Chemistry, University of Oxford**
Supervised 2nd year chemistry teaching laboratory and marked students based on good laboratory practice and written reports (15-20 students),
- Apr-May 2012 **Junior Laboratory Demonstrator, Department of Chemistry, University of Oxford**
Supervised 1st year chemistry and biochemistry teaching laboratory and marked students based on good laboratory practice and written reports (15-20 students),

ACADEMIC QUALIFICATION

- Oct 2009- Oct 2013 **DPhil, Organic Chemistry, University of Oxford**
Thesis title: Dynamic Combinatorial Mass Spectrometry for 2-oxoglutarate oxygenase inhibition
Designed and synthesised small molecule enzyme inhibitors of unprecedented potency and selectivity

Developed a novel dynamic combinatorial method employing native protein mass spectrometry (DCMS, Q-TOF), for inhibitor identification and optimisation
Developed and applied MS methods (MALDI-TOF, LCMS) to study cofactor, substrate and inhibitor binding

Used liquid chromatography (HPLC, UPLC) for analysis and purification of small molecules and peptides

Applied protein mutagenesis, expression and purification methods (FPLC, SDS page, dialysis) to generate novel constructs of recombinant enzymes

Supervised by Prof Christopher J. Schofield

Sep 2005- May 2009

BSc, Chemistry (2:1), University of Cyprus

Final year project: Synthesis and modification of Benzo[1,2,4]triazinones: Inhibitors of Amyloid- β Aggregation

Developed and applied new synthetic routes to small molecule heteroaromatic inhibitors

Supervised by Dr Panayiotis A. Koutentis

PROFESSIONAL DEVELOPMENT

May-Jun 2014 Teaching and Learning: Science not Magic, MPLS division, University of Oxford, UK.

Improve teaching effectiveness, Teaching methods and delivery in the digital age, Ethics

10-11 Feb 2011 Caprotec Workshop: Innovations in Small Molecule-Protein Interaction Analysis, Department of Chemistry, University of Oxford, UK.

Methods on biomolecule capture using molecular probes

22 Mar 2010 Postgraduate Skills Training Office: Foundations for a Successful DPhil, MPLS division, University of Oxford, UK.

Time-management, Work relations, Ethics, Career development

TEACHING

Philosophy

My teaching philosophy involves encouraging young scientists to realise their potential and shortcomings so that they achieve their best. I try, with the use of challenging problems and/or life examples, to keep their interest in the subject and to motivate them to self-learn.

Experience

Oct 09-May 2010 Voluntary teaching of school students (1-2 students), OxfordHub, University of Oxford.

Helping students with reading or mathematical problems through exercise

Sep-Dec 2008 Teaching assistant, Supervised 3rd year Organic Chemistry discussion group (15 students), Department of Chemistry, University of Cyprus.

Problem solving and explanation of complicated topics in Organic chemistry

AREAS of SCIENTIFIC EXPERTISE

General Area of Research	Pharmaceutical Chemistry/Drug Discovery
Disease and Conditions	Cancer, Cardiovascular Disease Alzheimer's, Obesity
Experimental Research	Dynamic Combinatorial Chemistry (DCC) Synthesis of aromatic compounds Structure Activity Relation studies Mass Spectrometry Enzyme purification <i>In vitro</i> assay development

ADDITIONAL SKILLS

- Proper and safe laboratory practice in the Department of Biochemistry. Informing students, production of written COSHH forms according to European legislation and handling of lab chemicals. Francis Barr Group, University of Oxford
- Supervision of the project "Inhibition and mechanistic studies on DNA and RNA demethylases". Role included outlining the project aims, directing the research and time management, as well as supervising and mentoring two MSc and two DPhil students in synthesis and enzymology, Schofield Group, University of Oxford
- Supervision of Q-TOF mass spectrometer instrument. Training of postdoctoral, doctoral and master students and responsible for the booking and use of the instrument between 40 people, Christopher Schofield Group, University of Oxford

LECTURES

1. Demetriades M. Dynamic Combinatorial Mass Spectrometry: a powerful tool for quick identification of selective 2-oxoglutarate oxygenases inhibitors
Department of Chemistry, University of Cyprus, Lefkosia, Cyprus, May 23, 2014
2. Demetriades M. Dynamic Combinatorial Mass Spectrometry: a powerful tool for quick identification of selective 2-oxoglutarate oxygenases inhibitors
"32th Cyprus-Noordwijkerhout-Camerino Symposium Trends in Drug Research, Limassol, Cyprus, May 18-22, 2014
3. Demetriades M, Leung IK, Chowdhury R, Woon EC, Chan MC, Claridge TD, Schofield CJ. Dynamic Combinatorial Mass Spectrometry for the identification of potent enzyme inhibitors
St Peter's College "Grad Fest 2012", Oxford, UK, November 13, 2012 (Poster presentation).
4. Demetriades, M. Boronic acid/ester Dynamic Combinatorial Chemistry for Prolyl Hydroxylase Domain 2 Inhibition
Department of Chemistry 3rd year graduate talks, Oxford, UK, October 4, 2012.
5. Demetriades, M. Improving the drug discovery process
St. Peter's College Graduate Seminars, Oxford, UK, November 29, 2011.

6. Demetriades M, Leung IK, Chowdhury R, Woon EC, Chan MC, Claridge TD, Schofield CJ. Use of Dynamic Combinatorial Mass Spectrometry to identify potent Prolyl Hydroxylase 2 inhibitors
Pfizer Organic Chemistry Symposium and Poster Competition, Oxford, UK, October 20, 2011.
7. Demetriades M, Leung IK, Chowdhury R, Woon EC, Chan MC, Claridge TD, Schofield CJ. Use of Dynamic Combinatorial Mass Spectrometry to identify potent Prolyl Hydroxylase 2 inhibitors
"29th Cyprus-Noordwijkerhout-Camerino Symposium Trends in Drug Research, Limassol, Cyprus, October 2-7, 2011 (Poster presentation).
8. Demetriades, M. Dynamic Combinatorial Chemistry in Drug Discovery
St Peter's College "Grad Fest 2010", Oxford, UK, November 2, 2010.

POSSITIONS of RESPONSIBILITY

Elected for two years as the treasurer of the St. Peter's College graduate community (MCR) committee. MCR budget presentation in College meetings and managed to increase funding to renovate facilities.

AWARDS

Sep 2009 Award on Research Competition For Students
By **Research Promotion Foundation Cyprus**
Project: "Synthesis and modification of Benzo[1,2,4]triazinones: Inhibitors of Amyloid- β Aggregation".

List of Publications (h-index 10)

1. Demetriades, M., Shishodia, S., Zhang, D., Aik, W., Leung IKH., Tumber, A., Lesniar, R., Kawamura, A., McDonough, M., Schofield, C.J., Structure assisted design of a highly selective FTO inhibitor. *JACS* (subm).
2. Karuppagounder SS, Alim I, Khim SJ, Bourassa MW, Sleiman SF, John R, Thinnas CC, Yeh TL, Demetriades M, Neitemeier S, Cruz D, Gazaryan I, Killilea DW, Morgenstern L, Xi G, Keep RF, Schallert T, Tappero RV, Zhong J, Cho S, Maxfield FR, Holman TR, Culmsee C, Fong GH, Su Y, Ming GL, Song H, Cave JW, Schofield CJ, Colbourne F, Coppola G, Ratan RR.' Therapeutic targeting of oxygen-sensing prolyl hydroxylases abrogates ATF4-dependent neuronal death and improves outcomes after brain hemorrhage in several rodent models. *Sci Transl Med*, **2016**, 328-45.
3. Chan, M.C., Atasoylu, O., Hodson, E., Tumber, A., Leung, I.K.H., Chowdhury, R., Gómez-Pérez, V., Demetriades, M., Rydzik, A.M., Holt-Martyn, J., Tian Y.M., Bishop, T., Claridge, T.D.W., Kawamura, A., Pugh, C.W., Ratcliffe, P.J., Schofield, C.J., Potent and Selective Triazole-based Inhibitors of the Hypoxia-inducible Factor Prolyl-hydroxylases with Activity in the Murine Brain. *PLoS One*, **2015**, e0132004.
4. McMurray, F., Demetriades, M., Aik, W., Merkestein, M., Kramer, H., Andrew, D.S., Scudamore, C.L., Hough, T.A., Wells, S., Ashcroft, F.M., McDonough, M.A., Schofield, C.J., Cox, R.D., Pharmacological Inhibition of FTO. *PLoS One*, **2015**, e0121829.
5. Xu, C., Liu, K., Tempel, W., Demetriades, M., Aik, W., Schofield, C.J., Min, J., Structures of human ALKBH5 demethylase reveal a unique binding mode for specific single-stranded N6-methyladenosine RNA demethylation. *J Biol Chem*, **2014**, 20, 17299-311.
6. Aik, W., Scotti, J.S., Choi, H., Gong, L., Demetriades, M., Schofield, C.J., and McDonough, M.A., Structure of human RNA N6-methyladenine demethylase ALKBH5 provides insights into its mechanisms of nucleic acid recognition and demethylation. *Nucleic Acids Res*, **2014**, 4741-53.
7. Cherblanc, F.L., Chapman, K.L., Reid, J., Borg, A.J., Sundriyal, S., Alcazar-Fuoli, L., Bignell, E., Demetriades, M., Schofield, C.J., Dimaggio, P.A.J., Brown, R., and Fuchter, M.J., On the Histone Lysine Methyltransferase Activity of Fungal Metabolite Chaetocin. *J Med Chem*, **2013**, 56, 8616-25.
8. Valegard, K., Iqbal, A., Kershaw, N.J., Ivison, D., Genereux, C., Dubus, A., Blikstad, C., Demetriades, M., Hopkinson, R.J., Lloyd, A.J., Roper, D.I., Schofield, C.J., Andersson, I., and McDonough, M.A., Structural and mechanistic studies of the orf12 gene product from the clavulanic acid biosynthesis pathway. *Acta Crystallogr D*, **2013**, 69, 1567-79.
9. Aik, W., Demetriades, M., Hamdan, M.K.K., Bagg, E.A.L., Yeoh, K.K., Lejeune, C., Zhang, Z.H., McDonough, M.A., and Schofield, C.J., Structural Basis for Inhibition of the Fat Mass and Obesity Associated Protein (FTO). *J Med Chem*, **2013**, 56, 3680-8.
10. Bishop, T., Talbot, N.P., Turner, P.J., Nicholls, L.G., Pascual, A., Hodson, E.J., Douglas, G., Fielding, J.W., Smith, T.G., Demetriades, M., Schofield, C.J., Robbins, P.A., Pugh, C.W., Buckler, K.J., and Ratcliffe, P.J., Carotid body hyperplasia and enhanced ventilatory responses to hypoxia in mice with heterozygous deficiency of PHD2. *J Physiol-London*, **2013**, 591, 3565-77.
11. Chowdhury, R., Candela-Lena, J.I., Chan, M.C., Greenald, D.J., Yeoh, K.K., Tian, Y.M., McDonough, M.A., Tumber, A., Rose, N.R., Conejo-Garcia, A., Demetriades, M., Mathavan, S., Kawamura, A., Lee, M.K., van Eeden, F., Pugh, C.W., Ratcliffe, P.J., and Schofield, C.J.,

Selective Small Molecule Probes for the Hypoxia Inducible Factor (HIF) Prolyl Hydroxylases. *Acs Chem Biol*, **2013**, 8, 1488-96.

12. Leung, I.K.H., Demetriades, M., Hardy, A.P., Lejeune, C., Smart, T.J., Szollossi, A., Kawamura, A., Schofield, C.J., and Claridge, T.D.W., Reporter Ligand NMR Screening Method for 2-Oxoglutarate Oxygenase Inhibitors. *J Med Chem*, **2013**, 56, 547-55.
13. Yeoh, K.K., Chan, M.C., Thalhammer, A., Demetriades, M., Chowdhury, R., Tian, Y.M., Stolze, I., McNeill, L.A., Lee, M.K., Woon, E.C.Y., Mackeen, M.M., Kawamura, A., Ratcliffe, P.J., Mecinovic, J., and Schofield, C.J., Dual-action inhibitors of HIF prolyl hydroxylases that induce binding of a second iron ion. *Org Biomol Chem*, **2013**, 11, 732-45.
14. Catto, M., Berezin, A.A., Lo Re, D., Loizou, G., Demetriades, M., De Stradis, A., Campagna, F., Koutentis, P.A., and Carotti, A., Design, synthesis and biological evaluation of benzo[e][1,2,4]triazin-7(1H)-one and [1,2,4]-triazino[5,6,1-jk]carbazol-6-one derivatives as dual inhibitors of beta-amyloid aggregation and acetyl/butyryl cholinesterase. *Eur J Med Chem*, **2012**, 58, 84-97.
15. Demetriades, M., Leung, I.K.H., Chowdhury, R., Chan, M.C., McDonough, M.A., Yeoh, K.K., Tian, Y.M., Claridge, T.D.W., Ratcliffe, P.J., Woon, E.C.Y., and Schofield, C.J., Dynamic Combinatorial Chemistry Employing Boronic Acids/Boronate Esters Leads to Potent Oxygenase Inhibitors. *Angew Chem Int Ed*, **2012**, 51, 6672-5.
16. Woon, E.C.Y., Demetriades, M., Bagg, E.A.L., Aik, W., Krylova, S.M., Ma, J.H.Y., Chan, M.C., Walport, L.J., Wegman, D.W., Dack, K.N., McDonough, M.A., Krylov, S.N., and Schofield, C.J., Dynamic Combinatorial Mass Spectrometry Leads to Inhibitors of a 2-Oxoglutarate-Dependent Nucleic Acid Demethylase. *J Med Chem*, **2012**, 55, 2173-84.