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CAREER HIGHLIGHTS

- ***Senior Lecturer in Medicinal Chemistry***
  Cardiff University, UK
  Aug. 2018- present.
- ***Lecturer in Medicinal Chemistry***
  University of Birmingham/Cardiff University, UK
  March 2013- July. 2018.
- ***Fellow of The Higher Education Academy***
  July 2016.
- ***MRC Career Development Fellow***
  Protein Phosphorylation Unit, Medical Research Council, UK
  Aug. 2010 – Feb. 2013.
  Advisor: Prof. Dario R. Alessi FRS
- ***Postdoctoral Research Associate***
  The Biodesign Institute, Arizona State University, USA
  Feb. 2009 – May 2010.
  Advisor: Prof. Sidney M. Hecht
- ***Ph.D. in Medicinal Chemistry***
  Cardiff School of Pharmacy and Pharmaceutical Sciences,
  Cardiff University, UK
  Oct. 2005 - Dec. 2008.
  Advisor: Prof. Chris McGuigan
- ***Master in Pharmacy (MPharm)***
  Department of Pharmacy, King's College London, UK.
  Sep. 2001 - Jul. 2005.
  Advisor: Prof. Robert C. Hider

PATENTS

- Tucker, J. H. R.; Nguyen, H. V.; Hodges, N.; **Mehellou, Y.;** Tselepis, C. Invention: "Ferrocenyl nucleosides as nucleoside analogues and uses thereof".
  Publication number: WO2015092432 A1.
- Muqit, M. M. and **Mehellou, Y.** Invention: "Small molecule PINK1 activators".
- **Mehellou, Y.;** Willcox, B. E. "Phosphoantigen Prodrugs". *Patent filled.*

RESEARCH SUCCESS HIGHLIGHTS

- Evaluation of a clinically used drug as a potent activator of PINK1 kinase in cells and in neurons.
- Discovery of a nucleoside and its monophosphate prodrug as an activator of PINK1 and thus have potential to treat Parkinson's disease.
- Discovery of small molecule prodrugs as potent activators of a subtype of immune cells, which are involved in cancer immunosurveillance.
- Discovery of the allosteric site that regulates the function of SPAK and OSR1 kinases.

RESEARCH FUNDING

- *Funding:* MRC, Wellcome Trust, Lily Foundation, BBSRC/AstraZeneca and EPSRC.

CURRENT LAB

- *Lab members:* 7 PhD students and 2 Postdocs.

PUBLICATIONS

1. **Mehellou, Y.*;** AlAmri, M. A.; Dhiani, B. A.; Kadri, H. *C*-terminal phosphorylation of SPAK and OSR1 kinases promotes their binding and activation by the scaffolding protein MO25. *Biochem. Biophys. Res. Comm.* **2018**, DOI: 10.1016/j.bbrc.2018.07.128.
2. AlAmri, M. A.; Kadri, H.; Alderwick, L. J.; Jeeves, M.; **Mehellou, Y*.** The Photosensitizing Clinical Agent Verteporfin is an Inhibitor of SPAK and OSR1 Kinases. *ChemBioChem* **2018**, DOI: 10.1002/cbic.201800272.
3. Kadri, H.; Taher. T. E.; Xu, Q.; Bryan, R. T.; Willcox, B. E.; **Mehellou, Y***. Aryloxy Triester Phosphonamidates of Phosphoantigens Exhibit Favorable Stability and Potent Activation of Vγ9/Vδ2 T-Cells. *ChemRxiv* **2018**, DOI: 10.26434/chemrxiv.6755033.v1.
4. Kadri, H.; Lambourne, O. A.; **Mehellou, Y*.** Niclosamide, a drug with many (re)purposes. *ChemMedChem* **2018**, *13*, 1088-1091.
5. Davey, M. S.; Malde, R.; Mykura, R. C.; Baker, A. T.; Taher, T. E.; Le Duff, C. S.; Willcox, B. E.; **Mehellou, Y*.** Synthesis and Biological Evaluation of (*E*)-4-Hydroxy-3-Methylbut-2-enyl Phosphate (HMBP) Aryloxy Triester Phosphoramidate Prodrugs as Activators of Vγ9/Vδ2 T-Cell Immune Responses. *J. Med. Chem.* **2018**, *61*, 2111-2117.
6. Barini, E.; Miccoli, A.; Tinarelli, F.; Mulholland, K.; Kadri, H.; Khanim, K.; Stojanovski, L.; Read, K. D.; Burness, K.; Blow, J. J.; **Mehellou, Y*.**; Muqit, M. M. The anthelmintic drug niclosamide and its analogues activate the Parkinson's disease associated kinase PINK1. *ChemBioChem* **2018**, *19*, 425-429.
7. AlAmri, M.A.; Kadri, H.; Dhiani, B.A.; Mahmood, S.; Elzwawi, A.; **Mehellou, Y***. WNK-Signaling Inhibitors as Potential New Antihypertensive Drugs. *ChemMedChem* **2017**, *12*, 1677-1686.
8. Salim, M.; Knowles, T.; Baker, A. T.; Davey, M. S.; Jeeves, M.; Sridha, P.; Wilkie, J.; Willcox, C. R.; Kadri, H.; **Mehellou, Y.**; Mohammed, F.; Willcox, B. E. BTN3A1 discriminates γδ T cell phosphoantigens from non-antigenic small molecules via a conformational sensor in its B30.2 domain. *ACS Chem. Biol.* **2017**, DOI: 10.1021/acschembio.7b00694.
9. **Mehellou, Y*.**; Singh, H.; Balzarini, J. The ProTide prodrug technology: From the concept to the clinic. *J. Med Chem.* **2017**, DOI: 10.1021/acs.jmedchem.7b00734.
10. AlAmri, M. A.; Kadri, H.; Alderwick, L. J.; Simpkins, N. S.; **Mehellou, Y***. Rafoxanide and Closantel inhibit SPAK and OSR1 kinases by binding to a highly conserved allosteric site on their C-terminal domains. *ChemMedChem* **2017**, 12(9), 639-645.
11. Osgerby, L.; Lai, Y. C.; Thornton, P. J.; Amalfitano, J.; Le Duff, C. S.; Jabeen, I.; Kadri, H.; Miccoli, A.; Tucker, J. H. R.; Muqit, M. M. K.; **Mehellou. Y***. Kinetin riboside and its ProTides activate the Parkinson's disease associated PTEN-induced putative kinase 1 (PINK1) independent of mitochondrial depolarisation. *J. Med. Chem.* **2017**, 60(8), 3518-3524.
12. Kadri, H.; AlAmri, M. A.; Navratilova, I. H.; Alderwick, L. J.; Simpkins, N. S.; **Mehellou, Y***. Towards the development of small molecule MO25-binders as potential indirect SPAK/OSR1 kinase inhibitors. *ChemBioChem* **2017**, 18(5):460-465.
13. Kedge, J. L.; Nguyen, H. V.; Khan, K.; Male, L.; Ismail, M. K.; Roberts, H. V.; Hodges, N. J.; Horswell, S. L.; **Mehellou, Y.**; Tucker, J. H. R. Organometallic Nucleoside Analogues: Effect of

Hydroxyalkyl Linker Length on Cancer Cell Line Toxicity. *Eur. J. Inorg. Chem.* **2017**, 466–476.
14. Thornton, P.J.; Kadri, H.; Miccoli, A.; **Mehellou, Y***. Nucleoside Phosphate and Phosphonate Prodrug Clinical Candidates. *J. Med. Chem.* **2016**, 59(23), 10400-10410.
15. **Mehellou, Y***. The ProTides Boom. *ChemMedChem* **2016**, 11(11), 1114-1116.
16. Butterworth, S.; **Mehellou, Y.;** Rainger, P.; Thomas, S.; Mason, J.; Jagpal, P.; Cox, A.; Marriott, J. Design and Development of Virtual Chemistry Practicals for Pharmacy Students. Manchester Pharmacy Education Conference; 29 Jun **2015**.
17. Nguyen, H. V.; Sallustrau, A.; Balzarini, J.; Bedford, M. R.; Eden, J. C.; Georgousi, N.; Hodges, N. J.; Kedge, J.; **Mehellou, Y**.; Tselepis, C.; Tucker, J. H. Organometallic nucleoside analogues with ferrocenyl linker groups: synthesis and cancer cell line studies. *J. Med. Chem.* **2014**, 57(13), 5817-22.
18. Rainger, P.; **Mehellou, Y.;** Mason, J. Teaching Peptide and Oligo synthesis in a Virtual Lab with gamefification and integrated clinical scenarios. *SEB Education and Public Affairs Section Symposium* **2014**, EPA14.28, Society of Experimental Biology.
19. Ohta, A.; Schumacher, F. R.; **Mehellou, Y**.; Johnson, C.; Knebel, A.; Macartney, T. J.; Wood, N. T.; Alessi, D. R.; Kurz, T. The CUL3-KLHL3 E3 ligase complex mutated in Gordon's hypertension syndrome interacts with and ubiquitylates WNK isoforms: disease-causing mutations in KLHL3 and WNK4 disrupt interaction. *Biochem. J.* **2013**, 451(1), 111-122.
20. **Mehellou, Y*.;** Alessi, D. R.; Macartney, T. J.; Szklarz, M.; Knapp, S.; Elkins, J. M. Structural insights into the activation of MST3 by MO25. *Biochem. Biophys. Res Commun.* **2013**, 431(3), 604-609.
21. Chen, S.; Fahmi, N. E.; Nangreave, R. C.; **Mehellou, Y**.; Hecht, S. M. Synthesis of pdCpAs and transfer RNAs activated with thiothreonine and derivatives. *Bioorg. Med. Chem.* **2012**, 20(8), 2679-2689.
22. Thastrup, J. O.; Rafiqi, F. H.; Vitari, A. C.; Pozo-Guisado, E.; Deak, M.; **Mehellou, Y**.; Alessi, D. R. SPAK/OSR1 regulate NKCC1 and WNK activity: analysis of WNK isoform interactions and activation by T-loop trans-autophosphorylation. *Biochem. J.* **2012**, 441(1), 325-337.
23. Filippi, B. M.; de los Heros, P.; **Mehellou, Y**.; Navratilova, I.; Gourlay, R.; Deak, M.; Plater, L.; Toth, R.; Zeqiraj, E.; Alessi, D. R. MO25 is a master regulator of SPAK/OSR1 and MST3/MST4/YSK1 protein kinases. *EMBO J.* **2011**, 30(9), 1730-1741.
24. **Mehellou Y***. Phosphoramidate prodrugs deliver with potency against hepatitis C virus. *ChemMedChem.* **2010**, 5(11), 1841-1842.
25. **Mehellou Y**, Valente R, Mottram H, Walsby E, Mills KI, Balzarini J, McGuigan C.Phosphoramidates of 2'-beta-D-arabinouridine (AraU) as phosphate prodrugs; design, synthesis, in vitro activity and metabolism. *Bioorg. Med. Chem.* **2010**, 18(7), 2439-2446.
26. **Mehellou Y**, Balzarini J, McGuigan C. The design, synthesis and antiviral evaluation of a series of 5-trimethylsilyl-1-beta-D-(arabinofuranosyl)uracil phosphoramidate ProTides. *Antiviral Chem. Chemother.* **2010**, 20(4), 153-160.
27. **Mehellou Y***, De Clercq E. Twenty-six years of anti-HIV drug discovery: where do we stand and where do we go? *J. Med. Chem.* **2010**, 53(2), 521-538.
28. **Mehellou Y**, Balzarini J, McGuigan C. Aryloxy phosphoramidate triesters: a technology for delivering monophosphorylated nucleosides and sugars into cells. *ChemMedChem.* **2009**, 4(11), 1779-1791.
29. **Mehellou, Y.**; Balzarini J, McGuigan C. An investigation into the

anti-HIV activity of 2',3'-didehydro-2',3'-dideoxyuridine (d4U) and 2',3'-dideoxyuridine (ddU) phosphoramidate 'ProTide' derivatives. *Org. Biomol. Chem.* **2009**, 7(12), 2548-2553.

30. **Mehellou, Y**.; McGuigan C, Brancale A, Balzarini J. Design, synthesis, and anti-HIV activity of 2',3'-didehydro-2',3'-dideoxyuridine (d4U), 2',3'-dideoxyuridine (ddU) phosphoramidate 'ProTide' derivatives. *Bioorg. Med. Chem. Lett.* **2007**, 17(13), 3666-3669.
31. **Mehellou, Y.**, McGuigan, C. and Balzarini, J. The design, synthesis and Anti-HIV activity of a selected group of 2 ',3 '-didehydro-2 ',3 '-dideoxyguanosine (d4G) and 2 ',3 '-dideoxyguanosine (ddG) 'ProTide' derivatives. *Antiviral Res.* **2007**, 74(3), 50.

SELECTED PRESENTATIONS

- "Mining Kinase Signaling Pathways for Drug Discovery Opportunities". Postgraduate Symposium XI: Biological and Bedicinal Chemistry Symposium for Postgraduates. Cambridge University, 8th December **2017**.
- "Manipulating Cell Signaling Cascades by Sneaking Phosphates into Cells". The 17th RSC Chemical Biology and Bioorganic Group (CBBG) Firbush conference, 8th-10th September **2017**.
- "Sneaking phosphates into cells: a powerful strategy in drug discovery." Presentation to the McGuigan group, School of Pharmacy, Cardiff University, 2nd February **2016**.
- "Development of STAT3 dimerization inhibitors". November 27th, **2015**, Department of Biomedical Sciences, University of Sheffield.
- "My Pursuit of Cutting-Edge Science: From Nucleosides to Protein Engineering". *June 2nd,* **2010**. Medical Research Council, Protein Phosphorylation Unit, Dundee.
- "The Pursuit of Novel Antiviral Therapies: From Nucleosides to RNA-Binders and Stem Cells". *April 5th,* **2010**. School of Pharmacy, University of California, San Francisco.
- "The Design, Synthesis and Anti-HIV Activity of a Series of 2',3'-Didehydro-2',3'-Dideoxyuridine and 2',3'-Dideoxyuridine Phosphoramidate Prodrugs". Biological Chemistry, Chemical Biology & Medicinal Chemistry Postgraduate Symposium, Cambridge. *November 29th,* **2007**. Cambridge University, UK.
- "The Design, Synthesis and Anti-HIV Activity of a Series of 2',3'-Didehydro-2',3'-Dideoxyuridine and 2',3'-Dideoxyuridine Phosphoramidates". 20th International Conference for Antiviral Research. *April 29-3 May*, **2007**. Palm Springs, California, USA.

ORGANISING CONFERENCES

- "Protein-Protein interactions: from biochemistry to drug discovery and pharmacology" as a session in Pharmacology 2016, 11th-13th December **2017**. Co-oranised and co-chaired with Dr. Patrick Eyers, University of Liverpool.
- "Biochemical strategies in drug discovery and targeting" as a session in Pharmacology 2016, 13th-15th December **2016**. Co-oranised and co-chaired with Dr. Patrick Eyers, University of Liverpool.

OTHER

- Member of the Biochemical Society Clinical and Translational Panel [2018-Present].
- Member of the Biochemical Society Signalling Panel (V) [2013-2018].
- Member of the Biochemical Society.
- Associate Editor for Cogent Chemistry (2015-2017).
- Grant reviewer for the BBSRC, BHF and Parkinson's UK.
- Frequent reviewer for medicinal chemistry and biochemistry journals e.g. Journal of Medicinal Chemistry, Bioorganic and Medicinal Chemistry Letters, ChemMedChem.