

## **Background Information Document on the research interests of the PIs who are involved in the CamPSF initiative.**

### **Prof Laura Itzhaki**

Laura Itzhaki's research focuses on a class of proteins with very distinctive architectures, known as tandem-repeat proteins, whose simple modular architecture makes them uniquely amenable to rational redesign with applications in synthetic biology and molecular therapeutics.

Engineering mono- and multi-valent inhibitors on a modular scaffold.

Aurora Diamante, Piyush K. Chaturbedy, Pamela J. E. Rowling, Janet R. Kumita, Rohan S. Eapen, Stephen H. McLaughlin, Marc de la Roche, Albert Perez-Riba and Laura S. Itzhaki  
Chemical Science 12, 880. PMID:33623657. DOI <https://doi.org/10.1039/D0SC03175E>

### **Dr Paul Miller**

Paul Miller's research focuses on understanding the molecular mechanisms of ion channel modulation by small molecules, protein toxins and antibodies, using protein engineering, cryo-EM and electrophysiology.

Mechanisms of inhibition and activation of extrasynaptic alpha-beta GABAA receptors.

Kasaragod VB, Mortensen M, Hardwick SW, Wahid AA, Dorovykh V, Chirgadze DY, Smart TG, Miller PS.

Nature, 2022, Feb, 602(7897), p. 529-533. PMID: 35140402.

<https://www.nature.com/articles/s41586-022-04402-z>

### **Prof Marko Hyvönen**

Marko Hyvönen's research focuses on use of structural biology to both understand the function of proteins and to modulate them with small molecules. His group uses protein engineering to facilitate structural characterisation of proteins of interest and fragment-based and structure guided methods for the development of small molecule modulators of proteins. Selective inhibitors of the Aurora A-TPX2 protein-protein interaction exhibit in vivo efficacy as targeted anti-mitotic agents.

S. R. Stockwell, D. E. Scott, G. Fischer, E. Guarino, T. P. C. Rooney, T. Feng, T. Moschetti, R. Srinivasan, E. Alza, A. Asteian, C. Dagostin, A. Alcaide, M. Rocaboy, B. Blaszczyk, A. Higuero, X. Wang, M. Rossmann, T. R. Perrior, T. L. Blundell, D. R. Spring, G. McKenzie, C. Abell, J. Skidmore, M. Hyvönen, A. R. Venkitaraman. Journal of Medicinal Chemistry, 17:15521–15536 (2024). <https://doi.org/10.1021/acs.jmedchem.4c01165>

A small-molecule inhibitor of the BRCA2-RAD51 interaction modulates RAD51 assembly and potentiates DNA damage-induced cell death.

D. E. Scott, N. J. Francis-Newton, M. E. Marsh, A. G. Coyne, G. Fischer, T. Moschetti, A. R. Bayly, T. D. Sharpe, K. T. Haas, L. Barber, C. R. Valenzano, R. Srinivasan, D. J. Huggins, M. Lee, A. Emery, B. Hardwick, M. Ehebauer, C. Dagostin, A. Esposito, L. Pellegrini, T. Perrior, G. McKenzie, T. L. Blundell, M. Hyvönen, J. Skidmore, A. R. Venkitaraman, C. Abell. Cell Chemical Biology, 28: 1–13, 2020. <https://doi.org/10.1016/j.chembiol.2021.02.006>

### **Prof Florian Hollfelder**

Florian Hollfelder's research focuses on gaining a fundamental understanding of the principles responsible for molecular recognition processes in chemistry and biology, in

particular whether these principles enable us to describe, manipulate and ultimately make functional molecules.

Evolution of protease activation and specificity via alpha-2-macroglobulin-mediated covalent capture.

Knyphausen, P.; Rangel Pereira, M.; Brear, P.; Hyvonen, M.; Jermutus, L.; Hollfelder, F. *Nat Commun* 2023, 14, 768. PMID: 36765057 or DOI: 10.1038/s41467-023-36099-7

### **Prof Mark Howarth**

Inspired by extraordinary molecular features from the natural world, our research develops new approaches for disease prevention and therapy. By engineering and evolving proteins and cellular systems, our projects range from fundamental analysis of protein interactions through to clinical application.

Multiviral Quartet Nanocages Elicit Broad Anti-Coronavirus Responses for Proactive Vaccinology.

Hills RA, Kit Tan T, Cohen AA, Keeffe JR, Keeble AH, Gnanapragasam PNP, Storm KN, Hill ML, Liu S, Gilbert-Jaramillo J, Afzal M, Napier A, James WS, Bjorkman PJ, Townsend AR, Howarth M.

bioRxiv. 2023 Feb 24:2023.02.24.529520. doi: 10.1101/2023.02.24.529520. Preprint. PMID: 36865256

### **Dr Catherine Wilson**

Catherine Wilson's research focuses on understanding the role of the Myc protein in heart cell regeneration and cancer, using genetic manipulations and degrader engineering.

Reactivation of Myc transcription in the mouse heart unlocks its proliferative capacity (2020). Bywater MJ, Burkhart DL, Sabò A, Straube J, Pendino V, Hudson JE, Quaife-Ryan GA, Porrello ER, Rae J, Parton RG, Kress TR, Amati B, Littlewood TD, Evan GI\*, Wilson CH\*. *Nat Commun* 11(1):1827. PMID: 32286286

### **Dr Pietro Sormanni**

Dr Pietro Sormanni's research focuses on the development of innovative data-driven technologies of rational antibody design, to obtain antibodies against targets that have been challenging to access using conventional approaches, and to improve or predict biophysical properties crucial for the successful development of antibody therapeutics.

Automated optimisation of solubility and conformational stability of antibodies and proteins. Rosace A, Bennett A, Oeller M, Mortensen MM, Sakhnini L, Lorenzen N, Poulsen C, Sormanni P.

*Nat Commun*. 2023 Apr 6;14(1):1937. doi: 10.1038/s41467-023-37668-6. PMID: 37024501