MASTER «*In Silico* Drug Design»

Second Year

OFFER AN INTERNSHIP
year 2021 / 20212

in Silico
iS-DD
Drug Design
disease & therapy
new insight to

send to Pr Camproux
anne-claude.camproux@u-paris.fr

Name of the head of laboratory or company: Dr. Manuel Mayr

Adress : Vascular Proteomics Lab, James Black Center, King's British Heart Foundation Centre, School of Cardiovascular Medicine & Science, King's College London, 125 Coldharbour Lane, London SE5 9NU, UK

E-mail : manuel.mayr@kcl.ac.uk

 Name of training supervisor: Dr. Konstantinos Theofilatos

Phone number : +44 (0) 7752793326
E-mail : konstantinos.theofilatos@kcl.ac.uk

Specialty training :   Research   ☒   Professional   ☐

a few key words to describe the subject of training :

cardiovascular proteomics, structural bioinformatics, cross-linking proteomics, machine learning, statistical analysis

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Title of internship: Statistical analysis, bioinformatics and machine learning analysis of omics datasets for cardiovascular diseases research applications

this subject is a first step towards a thesis: Yes

Short text describing your project

Despite major advances in our understanding and treatment of cardiovascular disease (CVD), there are likely targets beyond the traditional lipid measurements that can better inform on diagnosis and prognosis of CVD. The current measurements for non-HDL-C and apoB-100 do not discriminate between LDL-C and other apoB-100 carrying lipoprotein particles, e.g. triglyceride-rich lipoproteins and lipoprotein (a). With established therapeutics for lipid lowering, the development of more refined assays that distinguish the different apoB-100 carrying lipoproteins particles is of high priority. Using state-of-the-art lipidomics and proteomics approaches [1, 2], we have identified a broader panel of apolipoproteins compared to the ones currently being measured in the clinic (apoB-100 and apoA1) as potential biomarkers for early detection and prognosis stratification in CVD. Prof. Mayr's lab has world leading facilities for Mass

Spectrometry Proteomics while they have recently applied these technologies in several projects including predicting the trajectories of Covid-19 Patients, identifying the impact of heart failure medications in heart proteome, identifying biosignatures for cardiovascular risk prediction and studying the protein changes in valnurable symptomatic plaques [3, 4]. The bioinformatics group of the vascular proteomics group, led by Dr. Theofilatos has implemented a group of proprietary tools for statistical, network and machine learning analyses and preprocessing of proteomics data. The first objective of this internship will involve training the student into using these pipelines, working on optimizing their implementations in python and applying them at several proteomics datasets for the identification of diagnostic, prognostic and therapeutic targets of cardiovascular diseases. The second objective of this internship involves the design and development of a computational structural bioinformatics pipeline for the processing and validation of crosslinking Mass Spectrometry data results for the most accurate reconstruction of protein-protein interaction networks. In particular, the main objective would be to reconstruct the protein-protein interaction network of lipoprotein particles, as was done in [5] for PCSK9 protein and its interactome, and validate them using modern docking and other structural bioinformatics and modelling methods.

References.

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2. Kaudewitz D, Skroblin P, Bender LH, Barwari T, Willeit P, Pechlaner R, Sunderland NP, Willeit K, Morton AC, Armstrong PC, Chan MV, Lu R, Yin X, Gracio F, Dudek K, Langley SR, Zampetaki A, de Rinaldis E, Ye S, Warner TD, Saxena A, Kiechl S, Storey RF, Mayr M. Association of microRNAs and YRNAs with platelet function. Circ Res. 2016;118:420-432.
3. Gutmann, C., Takov, K., Burnap, S. A., Singh, B., Ali, H., Theofilatos, K., ... & Mayr, M. (2021). SARS-CoV-2 RNAemia and proteomic trajectories inform prognostication in COVID-19 patients admitted to intensive care. Nature communications, 12(1), 1-17.
4. Joshi, A., Rienks, M., Theofilatos, K., & Mayr, M. (2021). Systems biology in cardiovascular disease: a multiomics approach. Nature Reviews Cardiology, 18(5), 313-330.
5. Burnap, S. A., Sattler, K., Pechlaner, R., Duregotti, E., Lu, R., Theofilatos, K., ... & Mayr, M. (2021). PCSK9 Activity Is Potentiated Through HDL Binding. Circulation research.