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Criblage Moléculaire : à la recherche de sondes chimiques d’intérêt en thérapie humaine

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The Human Proteome Project “*Grand Challenge*” - A function for every Human protein

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The Human Proteome Project (HPP) is the flagship project of the *Human Proteome Organization* (www.hupo.org). Its mission is to characterize all of the proteins encoded by the human genome. To date, the HPP has identified a mass spectrometry signature for one product per gene for 93.1% of the genes in the human genome. There currently remain nearly 1400 proteins corresponding to coding genes which have still not been characterized by mass spectrometry. These proteins are either weakly expressed, expressed only at key times in development or in difficult-to-access tissues or cells. The characterization of these so-called *Missing proteins* continues.

The HPP has now launched the *Grand Challenge* that aims to assign *a minima* a function to each protein. This project requires the involvement of biologists and clinicians in all fields, who are specialists for example of a biological function, an organ, a pathology, etc. and most of whom are far removed from the world of proteomics. The results of their work can be used by the HPP to achieve its objectives. All approaches and methods are possible, among which, those of chemical biology. Thus, the treatment of cells with drugs or any biologically active molecule, provided that a minimum of information is known, is considered relevant. The data will be used by the HPP, in collaboration with the teams that produce them, to help approach the biological function of proteins of interest.

In order to carry out a proof of concept with a view to funding requests from research organizations, *ChemBioFrance* has joined forces with the HPP as part of its *Grand Challenge*. Ongoing work involves characterizing the effect of biologically active molecules on the global proteome of cells. The selected molecules must act on an identified target in order to determine the signaling pathways downstream of this target, and thus make it possible to better characterize the function(s) of the target in cells. The cells must be of human origin and the target must be expressed endogenously. The first results will be presented here.

Suggestions de lecture : Adhikari et al., A high-stringency blueprint of the human proteome. Nat Commun 2020. Doi: 10.1038/s41467-020-19045-9; HPP Grand Challenge White paper