Ecole Doctorale des Sciences Fondamentales

Title of the thesis: Design and synthesis of heterocyclic compounds containing a pyrazole moiety. Study of their biological properties.

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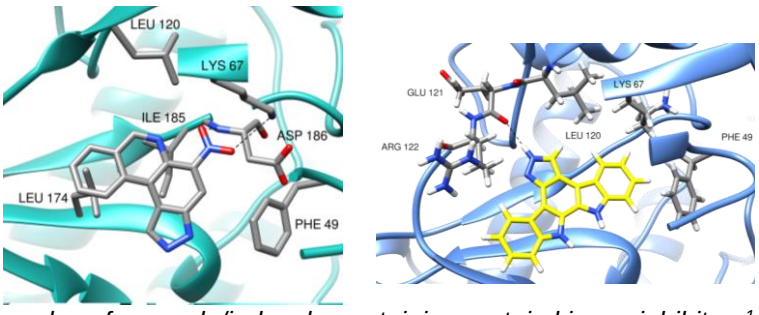
Summary :

Pyrazole and indazole are heterocyclic structure found in numerous small molecules with interesting biological activities. For example, these scaffolds can be part of protein kinase inhibitors. These enzymes catalyze the phosphorylation of substrate proteins in order to module their activity within cellular signaling pathways. Some pathologies such as cancer can be associated with an overexpression of some protein kinases, leading to the development of protein kinase inhibitors for therapy or as tools for biology.

The aim of this project is to design and synthesize novel protein kinase inhibitors containing a pyrazole or indazole moiety in order to gain in activity and selectivity for the target enzyme over other protein kinases.



Examples of pyrazole/indazole-containing protein kinase inhibitors[1,2]

In order to reach these objectives, the PhD student will use all necessary methods for the organic synthesis, purification and structural characterization of target molecules. The design and synthesis will be performed at the ICCF (Chemistry Institute of Clermont-Ferrand). Biological evaluations will be achieved in collaboration with biologist partners.

Références :

1. V. Suchaud, L. Gavara, F. Giraud, L. Nauton, V. Théry, **F. Anizon**, P. Moreau. Synthesis of pyrazolo[4,3-*a*]phenanthridines, a new scaffold for Pim kinase inhibition. *Bioorganic and Medicinal Chemistry* **2014**, *22*, 4704–4710.
2. Y.J. Esvan, F. Giraud, E. Pereira, V. Suchaud, L. Nauton, V. Théry, L.G. Dezhenkova, D.N. Kaluzhny, V.N. Mazov, A.A. Shtil, **F. Anizon**, P. Moreau. Synthesis and biological activity of pyrazole analogues of the staurosporine aglycon K252c. *Bioorganic and Medicinal Chemistry* **2016**, *24*, 3116–3124.