New 3-Mercaptopyruvate sulfurtransferase Inhibitors

Yan Berset

In plants and mammals, different types of endogenously produced molecules such as proteins, lipids or gases can carry information from one cell to another. Carbon monoxide (CO), nitric oxide (NO) and hydrogen sulfide (H_2S) belong to the family of the gasotransmitters. They are involved in many biological processes such as vasodilatation, cytoprotection, anti-inflammation or regulation of cardiovascular, nervous and immune system.

H_2S was initially determined as a gasotransmitter by Wang in 2002 and it has since attracted the interest of the scientific community. Even if research about H_2S has increased exponentially over the last decades, the exact biological role of this gas remains to be discovered.

In mammals, H_2S is produced by 3 different enzymes: cystathionine-β-synthase (CBS), cystathionine-γ-lyase (CSE) and 3-mercaptopyruvate sulfurtransferase (3-MST). In order to study the physiological role of H_2S, inhibitors of those 3 enzymes are required. Several CSE and CBS inhibitors (like propargylglycine (PAG) and β-cyano-L-alanine (BCA) for the former and aminooxyacetic acid (AOAA) for the latter) have already been reported. However, the research about a selective, potent and biologically suitable 3-MST inhibitor is still at the beginning. Hanaoka *et al*. reported in 2017 four 3-MST inhibitors, but their poor solubility in water makes them non-suitable for *in vivo* applications.

In this context, the aim of this project was to synthesize a library of potential inhibitors with diverse optimizations based upon one of the four original inhibitors shown below and to characterize their potency (3-MST inhibition) and selectivity (3-MST *vs.* CBS or CSE) *in vitro.*

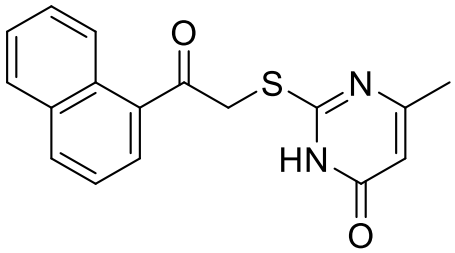

Figure 1: Original inhibitor reported by Hanaoka et al.

Prof. Christian G. Bochet