CYCLE DE CONFÉRENCES DE CHIMIE

Avec le concours de : Manufacture Française des Pneumatiques MICHELIN
Ecole Nationale Supérieure de Chimie de Clermont-Ferrand
Institut de Chimie de Clermont-Ferrand (ICCF UMR 6296)
U.F.R.S.T. / Master de Chimie / Département de Chimie

Jeudi 3 Mai 2012 à 16 h

Amphi de Chimie Paul REMI - (Site des Cézeaux)

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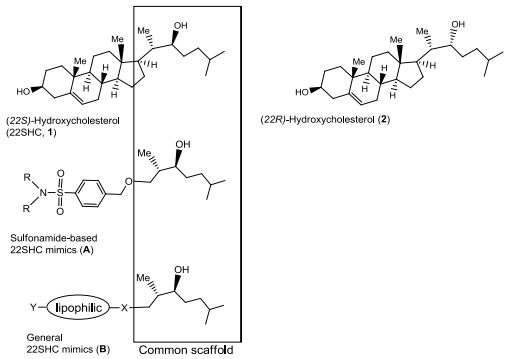
Synthesis and initial biological evaluation of new mimics of the LXR-modulator (*22S)*-hydroxycholesterol



Non-steroid 22SHC mimics. X = linker, Y = hydrogen-bonding group

Compounds that selectively modulate the LXR receptor to reduce lipogenesis and enhance glucose uptake without disturbing lipid homeostasis in liver, aim at a potential new class of drugs that can be used against type 2 diabetes (T2D) and obesity, which are major world-wide health challenges today [1]. (22*S*)-Hydroxycholesterol (22SHC, **1**), but not (22R)-hydroxycholesterol has been found to act as a LXR modulator in this way [2, 3]. The difference in biological action based on a single change in stereochemistry urged us to perform a synthetic programme aided by molecular modelling to identify new mimics of **1** that could represent lead candidates for drug development against T2D and obesity.

References

1. World-Health-Organization, *Diabetes*, in *Facts* 2006.
2. Kase, E.T., et al., *22-hydroxycholesterols regulate lipid metabolism differently than T0901317 in human myotubes.* Biochim Biophys Acta, 2006. **1761**(12): p. 1515-22.
3. Hessvik N.P., et al., *The liver X receptor modulator 22(S)-hydroxycholesterol exerts cell-type specific effects on lipid and glucose metabolism.* J. Steroid Biochem. Mol. Biol., 2011. Oct 25 [Epub ahead of print].

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