S15-4 Challenge of creating single-agents for the treatment of type 1 and 2 diabetes by targeting retinoid X receptor

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It might be seen as reckless to challenge to create single-agents for the treatment of both type 1 diabetes caused by the destruction of the Langerhans β cells in pancreas by excessive autoimmunity, and type 2 diabetes caused by the obesity. However, we hypothesized that retinoid X receptor (RXR) agonists, which are researched for the treatment of type 2 diabetes, will also act as novel anti-type 1 diabetes drugs based on the regulatory T cell (Treg) inducing activity which plays a key role on the immunotolerance maintenance. RXRs function as homo- or hetero-dimers with PPARs[1] or LXRs[2], which are reported to be associated with Treg induction. Interestingly, RXR agonists can activate these hetero-dimers even by themselves (permissive mechanism)[3]. Treg induction by RXR agonists, however, are little-known. Most known RXR agonists are lipophilc and have similar chemical structures. Since structurally different RXR agonists can activate these hetero-dimers differently[4], we have produced several new less lipophilic RXR agonists[5]. In this symposium, Treg inducing activity and efficacy to diabetes model mice by our RXR agonists will be presented.

References: 1) *J. Leukoc. Biol.* 2009, 86, 293−301. 2) *J. Leukoc. Biol.* 2009, 86, 401–409. 3) *Science* 2001, 294, 1866-1870. 4) *Biochem. Pharm.* 2008, 76, 1006–1013. 5) *ChemMedChem* 2008, *3*, 780-787.