

Poster presentation

A luminescence based biochemical assay for soluble guanylyl cyclase

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Soluble guanylyl cyclase (sGC) is a well-known target for the treatment of cardiovascular diseases. Finding activators of this enzyme is an important goal in pharmaceutical research labs.

The predominantly used method to determine the activity of soluble sGC biochemically is based on a radioactive assay format. This procedure is time-consuming, not feasible for uHTS and does not allow for online-monitoring of the reaction.

In order to be able to screen compound libraries and to investigate the kinetic behaviour of sGC activators a luminescence based assay for sGC was developed.

The assay is sensitive, robust and stable for over-night runs in screening. Reproducibility was checked in 384- and 1536-well plates. The assay allows for online-monitoring of the sGC reaction.

The potency of different kinds of activators like NO-donors, heme-dependend stimulators and heme-independend activators was determined. The influence of ODQ as a selective oxidizing reagent and SIN-1 as an NO-donor on the activation by stimulators and activators was checked. These two reagents were used to optimize the sensitivity of the assay in order to find new lead structures.

Results from the uHTS will be presented and compared to data generated with cell-based assays.