

## PA - - 8

2003年2月27日(木) 15:00~15:25

### High-Throughput Functional Screening (HTFS) of GPCRs

ユーロスクリーン社

Dr. Paolo Meoni

G protein-coupled receptors (GPCRs) constitute one of the largest protein families identified so far, and one of the most important sources of drug targets for the pharmaceutical industry. Potential drug candidates currently under development have been designed to modulate GPCRs activities in a number of different ways, to compensate for changes in receptor function following specific disease states. The choice of a functional, information-rich strategy for HTS of libraries against these targets is therefore a critical point in the definition of a successful drug-development campaign.

At Euroscreen, we have developed a number of possible approaches to make HTFS of GPCR a robust and economical alternative to the use of radioligand binding in screening campaigns. AequoScreen™ is a homogeneous, mix-and-read functional platform which was developed at Euroscreen and extensively tested in orphan receptor research. The Company has optimized the technology for the screening of small molecule libraries against validated GPCR targets. Results obtained from the combination of AequoScreen™ with several high-speed flash luminescence readers show the robustness and effectiveness of this technique for HTFS of GPCRs. Low levels of background emission from quiescent cells and the absence of toxic effect to the cells makes of AequoScreen an extremely sensitive and robust mix-and-read HTFS test for the screening of large libraries of agonist or antagonist compounds to receptors.

Calcium-optimized cell lines have also been developed to allow the use of calcium-sensing fluorescent techniques in the detection of the functional activity of GPCRs regardless of their physiological coupling to different transduction pathways.

Availability of optimized GPCR-cell lines for these techniques will prove to be a major advantage in the discovery of potential blockbuster drugs modulating the activity of such GPCRs in human pathophysiology.