

**Title:** SPR characterization of gastrin binders, for the development of anti-gastrin therapies in pancreatic cancer

**Authors:** Susana Shochat<sup>1</sup>, Rodrigo Barderas<sup>2</sup>, Martine J. Hollestelle<sup>3</sup>, Rob Meloen<sup>4</sup>, J. Ignacio Casal<sup>2</sup>, Jo W.M. Höppener<sup>3</sup>, Peter Timmerman<sup>4</sup>, Danièle Altschuh<sup>1</sup>

**Company / Institute:** 1 UMR 7175-LC1, CNRS/ULP, ESBS, Parc d'Innovation, Bld S. Brant, BP10413, 67412 Illkirch Cedex, France. 2 Protein Technology Unit. Biotechnology Program. Spanish National Cancer Center CNIO. 28029 Madrid. Spain. 3 Department of Metabolic and Endocrine Diseases, University Medical Center Utrecht, Utrecht, The Netherlands. 4 Pepscan Systems, Lelystad, The Netherlands.

**Abstract:**

A key step in the drug development process is to select the most promising candidates at an early stage, for further in vitro and in vivo investigations. The quantitative characterization of target-candidate binding yields essential information, as illustrated here for the development of gastrin binders. Gastrin plays an important role in driving the progression of pancreatic cancer, a disease for which there is currently no cure. Recently a vaccine against gastrin was shown to double the survival time and to improve the quality of life of pancreatic cancer patients. Unfortunately not all individuals respond to the vaccine. Furthermore the slow development of antibodies is problematic in the case of this fast progressing disease. These problems might be circumvented by administration of therapeutic gastrin antagonists. For the purpose of developing antagonists, recombinant antibody fragments specific for gastrin were obtained, as well as synthetic binders, based on their CDRs (Complementarity Determining Regions) covalently coupled to a small chemical scaffold. The interaction parameters between gastrin and the recombinant or synthetic binders were quantified by surface plasmon resonance (SPR) using a Biacore instrument (Biacore AB, Uppsala, Sweden). The binders for which SPR analysis indicated slowest gastrin dissociation together with a monomeric behavior, also consistently showed highest neutralization capacity, as evaluated from an in vitro gastrin bioassay. These results illustrate the importance of a detailed characterization of target-candidate binding properties for decision-making in drug development.