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FCT FACULDADE DE CIÊNCIAS E TECNOLOGIA UNIVERSIDADE NOVA DE LISBOA

Chemistry Department

Glycan microarrays for ligand discovery

Macromolecular Crystallography Group

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requimte rede de química e tecnologia

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Objectives

- To establish a **glycan microarray laboratory at REQUIMTE** for glycan ligand discovery and to develop **novel designer glycan microarrays** derived from polysaccharide glycomes.
- To apply the **glycan microarrays in combination with X-ray crystallography** to study the specificities of **noncatalytic carbohydrate-binding modules (CBMs) of cellulolytic bacteria**, which exhibit important enzyme-targeting functions for efficient biodegradation of polysaccharides.
- To extend the approach to study **glycan-protein interactions** in other biological systems in human health and disease, namely **host-microbe interactions**, mechanisms of **immunity**, and **folding and quality control** of nascent proteins.

Methodology

• Glycan microarrays, whereby **glycan probes are robotically printed on solid supports** as microspots (Fig. 1), are **high-throughput screening tools** for glycan ligand discovery and evaluation of specificities for glycan-protein recognition systems that mediate important biological events in health and disease (Fig. 2).

• We will construct a **designer glycan microarray platform** (Fig. 3). Oligosaccharide sequences will be obtained by selective depolymerisation of targeted polysaccharides. The polysaccharides and oligosaccharides in the form of neoglycolipid probes will be immobilized on the nitrocellulose chips. The chips will be probed with targeted glycan binding proteins. Structural studies of the **glycan recognition by X-ray crystallography** will be used, to derive structural information of the glycan-protein interaction and to elucidate the **molecular determinants of glycan specificity** and recognition.

Expected Results

• To analyse the products of up to ~200 genes encoding novel CBM members of cellulolytic bacteria (e.g. Rumen bacteria). We expect to identify **different glycan-binding patterns** among the CBMs analysed and **identify oligosaccharide ligands** (Fig. 4). The combined approach has the potential to give a considerable number of **different protein structures**: novel CBMs, and CBMs in complex with oligosaccharide ligands.

• To establish the *proof of concept* of a **novel *H. pylori* glycan microarray platform** and use it as a tool to better understand interactions with the host (screening with host glycan binding proteins, serological analysis of human serum infected with *H. pylori* strains, monitoring antibodies elicited using glycan-based vaccines for *H. pylori* therapy).

• To characterize the **fine specificities** of bispecific antibodies **engineered to target and kill cancer cells.**

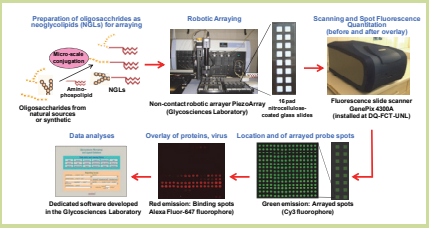

Fig.1: Glycan microarray system.

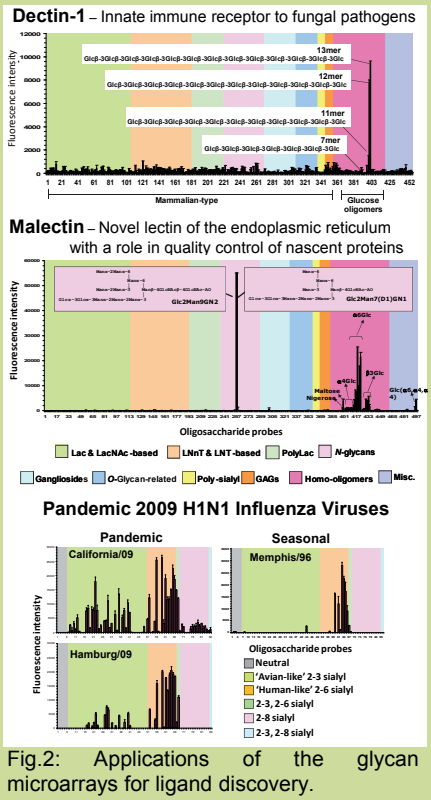

Fig.2: Applications of the glycan microarrays for ligand discovery.

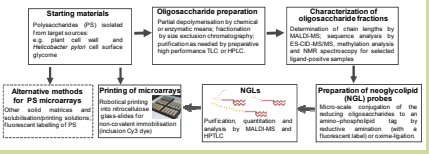

Fig.3: Approach for construction of the *designer* microarrays.

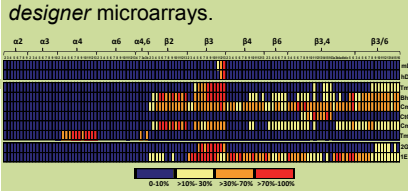

Fig.4: Patterns of binding of different glucan-binding proteins on the microarrays

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