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The comprehension of the molecular mechanisms at the basis of most autoimmune diseases is growing up, together with the need of simple diagnostic assays to detect autoantibodies as disease biomarkers. In this perspective, the selection of antigenic sources represents the key step for the set up of innovative immunoassays. The selection process moves from the identification of native antigens to the definition of autoepitopes. Peptides represent the ideal synthetic antigenic source and can guide the development of peptide-based immunoassays.
In particular, our aim is the identification and characterisation of the role of aberrant post-translational modifications (PTMs) of protein antigens involved in immune-mediated diseases identifying linear and/or conformational epitopes. **The final target of our project is the development of innovative diagnostic, prognostic tools using biophysical detection techniques (such as microcalorimetry and surface acoustic waves) to monitor disease activity. In particular the validation of these peptide-based diagnostics will be achieved by the correlation of the results with clinical data.** We focus our attention on the role of aberrant PTMs involved in the pathogenetic mechanisms of autoimmune diseases, and in particular those which involve sugars. A number of immune diseases have been associated with PTMs, which can alter the function and immunogenicity of protein antigens (Ags) by turning endogenous protein into potent antigens. In fact the PTM modified protein can become the antigen that stimulates the autoimmune response. Glycosylation is the most important PTM of secreted proteins and plays a crucial role in several immune functions. Because of the heterogeneity of the potential specific sites of glycosylation present on each protein and of the diversity of enzymes involved in protein glycosylation, the study is very demanding and the elucidation of the role of sugars is highly relevant to understand the disease at the molecular level .
The role of autoantibodies (autoAbs) in autoimmune diseases suggests that a distinct pattern of Multiple Sclerosis (MS) pathology could involve an Ab-mediated demyelination. An inter- and multidisciplinary effort of Prof. Papini and Prof. Lolli at Peptlab led to the development of a specific antigenic probe, CSF114(Glc) [1], a structure-based designed glycopeptide able to detect, isolate, and characterise specific autoAbs present in the sera of a statistically significant number of MS patients. CSF114(Glc) is the first reliable and efficient diagnostic/prognostic tool, that up to now demonstrated that an aberrant N-glycosylation is a fundamental determinant for autoAb recognition in MS. CSF114(Glc) is a family of peptides characterised by beta-hairpin structures exposing at the best a minimal epitope Asn(Glc). In fact a peptide represents an ideal antigenic target for immunoassays because it can easily be produced in high quality and quantity. Synthetic peptides are univocal antigenic sources characterized by a precise and definite chemical sequence moreover they can be used to introduce specific post-translational modifications or to stabilize the bioactive conformation.
An immunological study based on new PTM synthetic peptides will lead to select the best antigenic probes that will be used to develop new immunoassay. Moreover the selected synthetic probe will be instrumental to set up novel technological platform based on surface acoustic waves (SamX) or microcalorimetry (ITC200). A specific test will be developed to characterise antigen recognition by autoantibodies in a simple, rapid and reproducible way, with the possibility of simultaneous analysis of a large number of interactions. Thus identification of new autoantigens coupled to new detection techniques will allow a very precise analysis of the autoantibody profile of each patient**. Indeed, we will take profit of the presence of Prof. Lolli at UCP to improve our expertise on the analysis of the correlation between the results, obtained by the new biophysical techniques, and the clinical data from his patients.**

Moreover Prof Papini and Prof Lolli are collaborating to set up a multidisciplinary European network with the aim of submitting a project in the call "Future and Emerging Technologies (FET)" of Horizon 2020. To this aim they submitted this summer an MRSEI project (Montage De Reseaux Scientifiques Europeens Ou Internationaux) to ANR. The network, coordinated by Anna-Maria Papini will be based on a multidisciplinary expertise going from Chemistry & Physics to Biology & Medicine with applications in biomedical sciences (from bench to bedside).

[1] Granted USA & Australian Patent (n. 2002316989) .PCT WO 2003000733. Priority data FI2001A00011 Inventors: A.M. Papini, P. Rovero, M. Chelli, F. Lolli, a)*Nature Medicine* (2005) 11, 13. b)*Proc. Natl. Acad. Sci. U.S.A*. (2005) 102, 10273-10278. *c)J. Neuroimmunol*. (2005) 167, 131-137.d)*Neurology* (2005) *65*(5), 781-782.