



Basic and Translational Research in Rheumatic Diseases

Stefano Bombardieri

U.O. Reumatologia

Dipartimento di Medicina Clinica e Sperimentale

I. Study of new and old therapies in Systemic Lupus Erythematosus through experimental models: ongoing projects



Dr Chiara Tani, MD, PhD



P.I: Prof. Marta Mosca, MD, PhD
marta.mosca@med.unipi.it



Dr Sabrina Vagnani, PhD

Research Project	
Principal Investigator	<i>Marta Mosca</i>
Host Institution	Azienda Ospedaliera-Universitaria Pisana
Amount of founding	€ 90.000 University of Pisa, Bando CUCCS 2010 (Centro per l'Uso Clinico delle Cellule Staminali)
Collaborators	Dept of Clinical and Experimental Medicine (R Fazzi, S Pacini , A. Viridis, L. Ghiadoni, E. Duranti) Banca di Cellule e Tessuti- AOUP (Lapi S) Laboratorio Sequenziamento diretto, AOUP Immunpathologie -Charité-Campus Benjamin Franklin, Berlin



IA. Therapeutic role of mesenchymal stromal cells in systemic autoimmune diseases: results from a pre-clinical model of Systemic Lupus Erythematosus

Rationale: Mesenchymal stromal cells because of their immunomodulatory properties, are a promising new therapy in autoimmune disease; however, critical points needs to be still clarified before their use in humans.

SLE animal model: NZB/Wf1 mice

Results: systemic administration of allogenic bone marrow derived mesenchymal stromal cells improved renal parameters and immunological markers

Perspectives: Optimization of their use in animal models represents the necessary ground work for their use in Human SLE

Publications

C. Tani, et al. Ann Rheum Dis 2013

S. Vagnani et al. Ann Rheum Dis 2014



IB. Hydroxychloroquine in Systemic Lupus Erythematosus: therapeutic effects on renal biomarkers and endothelial function in a murine model

Rationale: Hydroxychloroquine has been historically used as an additional therapy in SLE. Clinical studies demonstrated a beneficial effect on cardiovascular prognosis, however the underlying mechanism of action is still poorly understood

SLE Animal Model: NZB/Wf1 mice

Results: chronic administration of hydroxychloroquine improves endothelial function at microvascular level and delays renal damage


Perspectives: This study results may offer novel insights for a rationale use of this old drug in rheumatic diseases

Publications

S. Vagnani, et al. Ann Rheum Dis 2013

II. Salivary proteomics as a unique tool for the Identification of Novel Biomarkers in Rheumatic Diseases

Rationale

- **Salivary glands** are **target organs** in most of the Rheumatic Diseases
 - **Salivary proteins** may closely **reflect the underlying pathogenetic process** in salivary glands
 - **Saliva is an ideal milieu for proteomic analysis** since:
 - the composition of saliva is much less complex than blood
 - it is much closer to where the action is
 - Salivary fluid can be easily collected
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- Salivary proteomic analysis may help to identify diagnostic, pathogenetic and therapeutic biomarkers for rheumatic diseases

Salivary proteomics as a unique tool for the Identification of Novel Biomarkers in Rheumatic Diseases

IIA. Proteomic analysis of whole saliva: a new tool for the identification of disease biomarkers in primary Sjögren's syndrome (pSS)



Research Project	
Principal Investigator	<i>Chiara Baldini</i>
Host Institution	Azienda Ospedaliera-Universitaria Pisana
Amount of founding	€ 250.000 (Ministero della salute_Bando giovani ricercatori 2009)
Collaborators	Dipartimento di Farmacia (prof. A Lucacchini) Biochimica (prof. R. Zucchi) NIH/NIDCR (dr. I. Alevizos)



Salivary proteomics as a unique tool for the Identification of Novel Biomarkers in primary Sjögren's Syndrome

Study population : pSS and sSS vs healthy volunteers and disease controls (RA, SSc, SLE)

Methods: Mass spectrometry techniques

Results:

- a reduction of proteins of acinar origin
(*i.e salivary amylases, carbonic anhydrase VI*)
- an increase of Immunoglobulins and inflammatory phase proteins
(*i.e calgranulins*)
- a correlation between secretory proteins and the salivary flow
(*i.e PIP, Cyst S*)

Publications

Giusti L. et al. Proteomics, 2007

Baldini C et al. Arthritis Res and Therapy, 2012

Gallo A et al. J Genet Syndr Gene Ther 2013

Salivary proteomics as a unique tool for the Identification of Novel Biomarkers in Rheumatic Diseases

IIB. Salivary proteomic analysis as a not invasive tool for the identification of biomarkers useful for diagnosis of fibromyalgic patients.



Research Project	
Principal Investigator	<i>Laura Bazzichi</i>
Host Institution	Azienda Ospedaliera-Universitaria Pisana
Amount of founding	€ 250.000 (Ministero della salute_Bando salute)
Collaborators	Dipartimento di Farmacia (prof. A Lucacchini)



Salivary proteomic analysis as a not invasive tool for the identification of biomarkers useful for diagnosis of FM

Study population : FM patients vs Healthy volunteers and Disease controls (RA, migraine)

Methods: Mass spectrometry techniques

Results:

- The analysis of the protein profiles allowed us to find
 - 26 spots with a different expression in FM respect to RA
 - 28 spots from the comparison of FM with migraine
 - 32 in FM respect to healthy subjects
- We found 7 spots differentially expressed exclusively in FM
- Six spots were identified as **serotransferrin** and the other as **alpha-enolase**

The top functions of these proteins:

Synthesis of reactive oxygen species
Cell movement of leukocytes
Inflammatory response
Glucose metabolism disorders
Mood disorders

Publications

Bazzichi L. Proteomics Clin Appl. et al. 2009
Giacomelli C. et al. Ann Rheum Dis 2014

II. Salivary proteomics as a unique tool for the Identification of Novel Biomarkers in Rheumatic Diseases

Rationale

PERSPECTIVES

Development of ELISA kits or Point of Care Technique for the non-invasive diagnosis and monitoring of patients with Rheumatic Diseases

From the perspective of the research salivary biomarkers could shed new lights on the pathogenesis underlying Rheumatic Diseases leading to develop new concepts for treatment modalities