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SUMMARY OF THESIS*

OLIVEIRA PINTO, Lucia Mendes de – Glicosaminoglicanos sintetizados por células mesangiais em modelo *in vitro* de nefropatia da IgA. São Paulo, 1998. (Tese de Doutoramento – Faculdade de Medicina da Universidade de São Paulo).

Glycosaminoglycans Sinthesized by Mesangial Cells in IgA Nephropathy in Vitro Model

Mesangial IgA glomerulonephritis is now well documented as the commonest form of idiopathic glomerulonephritis and is a major cause of endstage renal failure in most countries. It has a high risk for progression (20%) and effective treatment is not available. The etiology of IgA nephropathy is unknown. As in other progressive glomerulonephritis converge on a common avenue of sclerosis, by which specialized cellular structures are replaced by collagen and mesenchymal matrix. Currently there is much attention being drawn to the possible modulation role that proteoglycans jointly with growth factor exert on this process. Until now is not clear if the IgA deposition is noxious to the glomerulus or intrinsically pathophysiologically important.

This work started with the development of an experimental IgA nephropathy model in mice and further on by performing an *in vitro* simulation. The IgA fraction was purified out of the mice serum; thereupon its incorporation was checked by mice mesangial cells (MC) in culture, and caused a proliferative stimulus. Then the role of the experimental IgA fraction, monoclonal IgA (Sigma) and policlonal IgG (Sigma) on the glycosaminoglycans (GAG) synthesis by MC was evaluated by the measurement of ^{35}S absorption. For cultivation purposes two genetically selected lines of mice, for maximum and minimum acute inespecific inflammatory responses (AIRmax and AIRmin), were used.

It was found out that MC in culture synthesize heparan sulfate (HS) and dermatan sulfate (DS).On the other hand the MC coming from AIRmax lines synthesize more DS which is located in medium and matrix fraction. The experimental IgA fraction caused an HS increase in the cell fraction of the AIRmax cultivation. The IgG caused an increase of DS synthesized in both lines. The monoclonal IgA caused a severe GAG reduction due to the DS reduction in the medium in both lines.

Sequential studies are required to better characterize the effect of immunoglobulin on the GAG synthesized by MC and the potential intermediary link due to the stimulus on the liberation of growth factors and cytokines.

*This thesis is available at the Library of the Instituto de Medicina Tropical de São Paulo.

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41 (3): 150, May-June, 1999.

SUMMARY OF THESIS*

CARDI, Bruno Andrade – Avaliação do mecanismo de captação e endocitose de crotoxina submetida a ação da radiação gama, por macrófagos peritoneais de camundongos. São Paulo, 1999. (Tese de Doutoramento – Instituto de Pesquisas Energéticas e Nucleares, Autarquia associada à Universidade de São Paulo).

Study of Uptake and Endocytosis of Gamma Rays-Irradiated Crotoxin by Mice Peritoneal Macrophages

Purpose: To investigate the uptake and endocytosis of 2000Gy ^{60}Co irradiated crotoxin through mouse peritoneal macrophages, correlating with native one and another non related protein, the ovalbumin.

Material and methods: Native (CTXN) or 2000Gy ^{60}Co -rays (dose rate 540 Gy/hour) irradiated crotoxin (CTXI) or ovalbumin processed of same manner (OVAN-OVAI) were offered to mouse peritoneal macrophages and their uptake was evaluated by immunohistochemistry and quantitative *in situ* ELISA. The involvement of scavenger receptors (ScvR) was evaluated by using blockers drugs (Probuco-PBC or Dextran Sulfate-SD) or with nonspecific blocking using fetal calf serum (FBS).

Results: The morphology and viability of macrophages were preserved during the experiments. CTXI showed irradiation-induced aggregates, and formation of oxidative changes were observed on this protein after gamma rays treatment. By immunochemistry, we could observe heavy stained phagocytic vacuole on macrophages incubated with CTXI, as compared with CTXN. Quantitatively by *in situ* ELISA, the same pattern was observed, displaying a 2-fold CTXI incorporation. In presence of PBC or SD, we could find a significant decrease of CTXI uptake, but not of CTXN. However, the CTXN uptake was depressed by FBS, not observed with CTXI. OVA, after gamma rays treatment, underwent a high degradation suffering a potent incorporation and metabolism by macrophages, with a major uptake of OVAI in longer incubation (120 min).

Conclusions: Gamma rays (^{60}Co) produced oxidative changes on CTX molecule, leading to a uptake by ScvR-mice peritoneal macrophages, suggesting that the relation antigen-presenting cells and gamma rays-modified proteins are responsible for the better immune response presented by irradiated antigens.

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