ALBUMIN INDUCES RENAL DISEASE: ROLE OF mTOR PATHWAY

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Introduction and Objectives: The role of albumin in proximal tubule (PT) cells has emerged as one of the most important issues in renal physiology. Correlations between overload of albumin in the lumen of the PT, induction of a pro-inflammatory response, tubule-interstitial injury, and progression of renal disease have all been demonstrated. Data from the literature suggest an important role for mTORC1 in the development of a variety of renal diseases. However, some studies have shown that exposure to rapamycin can lead to glomerular injury when it is infused into healthy mice. Thus, in order to understand the progression of renal disease, it is crucial to understand the regulatory mechanism by which variations in albumin concentration in the PT affect the mTORC2/PKB/mTORC1 pathway under physiologic and pathophysiologic conditions.

Materials and Methods: The results presented were obtained in tubule-interstitial animal model and LLC-PK1 cells, a model of PT cells. Results: Our group showed that physiologic albumin concentrations activate the PI-3K/mTORC2/PKB/mTORC1/S6K pathway in LLC-PK1 cells, a model of PT cells. On the other hand, pathophysiologically high albumin concentrations inhibit mTORC2 activity and overactivate mTORC1 through an ERK/S6K/TSC2-dependent pathway. Our data also suggest that the expression of the megalin receptor on the luminal side of LLC-PK1 cells could serve as a sensor for variations in albumin concentrations under physiologic and pathophysiologic conditions.

Conclusion: Albumin overload promotes a mis-regulation of mTOR complexes. These effects could lead to the activation of NF-κB activity and secretion of pro-inflammatory chemokines involved in tubule-interstitial disease induced by albumin overload. These results help to elucidate the mechanism behind mTORC1 activation during renal disease.

Acknowledgement: This work was supported by grants from Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ), Instituto Nacional de Ciência e Tecnologia para Pesquisa Translacional em Saúde e Ambiente na Região Amazônica (INPeTAm/CNPq), and National Institutes of Health Grant.

Key Words: Albumin, Renal Disease, mTOR