

## Rosuvastatin-induced changes in mice kidney were remodeled by dietary essential amino acids supplementation

G. Corsetti<sup>1</sup>, C. Romano<sup>2</sup>, G. D'Antona<sup>3</sup>, E. Nisoli<sup>4</sup>, F.S. Dioguardi<sup>5</sup> and A. Stacchiotti<sup>1</sup>

<sup>1</sup> Department of Biomedical Sciences and Biotechnology, Human Anatomy Unit, University of Brescia, Brescia, Italy

<sup>2</sup> Department of Sport-Internal Medicine, University of Brescia, Brescia, Italy

<sup>3</sup> Department of Physiology, Human Physiology Unit, University of Pavia, Pavia, Italy

<sup>4</sup> Department of Pharmacology, Chemotherapy and Medical Toxicology, University of Milan, Milan, Italy

<sup>5</sup> Department of Internal Medicine, University of Milan, Milan, Italy

Rosuvastatin (Rvs) represents one of the most used cholesterol-lowering statins even if its effects may be wider than simply regulation of lipids metabolism [1]. Despite the efficacy in preventing cardiovascular diseases, long-term delivery of statins is associated to adverse effects [2]. So here we studied healthy normotensive mice fed with Rvs at a therapeutic dose (20 mg/kg/day) for one month. To evaluate the influence of dietary essential amino acids mixture (EAAM) in this model, other mice were fed with Rvs and EAAM daily for one month. A normal rodent chow or EAAM supplementation for the same period were further administered in control groups.

Ultrastructural analysis of the glomerular filtration barrier did not show any difference between groups. Glomerular area together with mitochondria and lysosomal parameters in renal tubules were evaluated. Moreover we focused on the distribution of chaperones and mitochondria markers (Grp75, Grp78, Bcl2), nitric oxide isoforms (iNOS and eNOS), and cell adhesion molecules (E-cadherin and  $\beta$ -catenin). Control groups were similar except for increased mitochondria density and Grp75 staining after EAAM diet. In contrast, Rvs attenuated Grp75/Bcl2 patterns, but enhanced Grp78 expression. Remarkably E-cadherin shifted from the basolateral to the apical side in proximal tubules while evident  $\beta$ -catenin signal was maintained mainly in the distal tubules and in the macula densa. However, after one month of EAAM supplementation, all parameters become almost similar to controls, except for Bcl2 that persisted at higher level.

These novel data suggest that, under basal conditions, Rvs may regulate proximal tubular polarity, lysosomes and mitochondria distribution. EAAM supplementation further reinforces the tubular structure in the kidney, stimulating mitochondriogenesis, as corroborated by morphometry, intense Bcl2 and vascular eNOS expressions. However to validate the efficacy of dietary of EAAM combined with Rvs therapy further studies on the renal function are mandatory.

### References

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