Research of early biomarkers of aneurysms, by metabonomic approach, and evaluation of the benefits of a multilayer flow modulator implant.

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1. Introduction

Aortic abdominal aneurysm is a common and silent vascular disease with a high risk of mortality due to its late and usually accidental diagnosis. Aneurysm treatment include surgery and stent implantation. In this context, Cardiatis (Isnes, Belgium) developed an original Multilayer Flow Modulator (MFM) implant. This stent is not expected to exclude the aneurysmal sac from the blood circulation but rather to change the flow from turbulent to laminar type inside the aneurysmal sac. This flow change is expected to stop the growth of the aneurysmal sac and lead to an organized thrombus formation inside the sac to completely fill it with progenitor circulating cells.

2. Approach

To find some new potential biomarkers of this pathology and acquire better knowledge on the underlying mechanism and to evaluate the possible benefits of a new concept of stent, we conducted a ^{1}H-NMR-based metabolomics study in rats. Metabolomics is a powerful tool to detect early signs of a nascent pathology from spectral changes due to alterations in biofluids metabolic compositions. This specific metabolic profile can further be used as a fingerprint of this pathology.

This study is based on samples collected from human patients and from a rat model of aneurysm. In this model, Spontaneously Hypertensive Rats (SHR) underwent surgery to develop, after 4 weeks, an aneurysm at the selected location.

This rat strain was preferred to best mimic the human pathology condition according to its important role in aneurysm expansion and rupture risks [1]. It was also an opportunity to study the dynamic metabolomic fingerprint of this spontaneously occurring hypertension.

3. Results

At the thirteenth week (time to develop spontaneaous hypertension in SHR rat), the comparison between urinary profile of SHR group and their control matches (Wistar Kyoto) shows a significant separation. Main metabolites involved in this group separation are citric acid cycle intermediates (alpha-ketoglurate, citric acid), trimethylamine N-Oxyde (TMAO), taurine (figure 1) and allantoin (from different models of PLS-DA, data not showed).

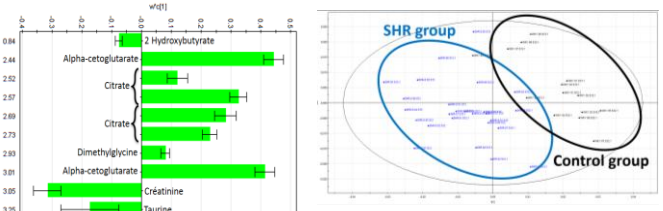

Figure 1. Scores plot with SHR rat in blue and their control matches (Wistar Kyoto) in black; Vip incriminated in their separation and their identifications (Increasing metabolites on the left and decreasing metabolites on the right in SHR urine sample)

4. Discussion

TMAO, allantoin and taurine levels are variating according to the literature during the onset of hypertension. Indeed, TMAO urinary level is an indicator of the onset of hypertension. This osmolyte has an important effect on hemodynamic response against angiotensin II [2].

As a result, the decrease in allantoin may reflect its arterial tension regulator effect, opposed to the onset of hypertension [3].

As shown by Akira and al [4], taurine exerts a significant stabilisation effect on blood pressure in SHR rats. Its increasing level could be related to a physiological response to the onset of hypertension.

Finally, levels of citric acid intermediates are decreasing following the appearance of hypertension. These changes would reflect a mitochondrial attack by the reactive oxygen species produced during the onset of this hypertension.

References

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