Protein Profiling and Discovery of Surrogate Markers of Vascular Remodeling in Murine Models for Hypertension by Mass Spectrometry

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Introduction

Hypertension: a clinical condition
- Hypertension is a common risk factor for cardiovascular diseases including myocardial infarction, coronary artery disease (CAD), renal failure, and stroke (Figure 1).
- Elevated blood pressure increases stress on arterial walls, causing aorta and coronary artery.
- Hypertension accelerates vascular remodeling and increases arterial wall thickness and expression of smooth muscle cells, hypertrophy, and extracellular matrix deposition (Figure 1, Table 1).

Methods

Four different treatments were applied in the study (Figure 2):
- Ang II (Angiotensin II): receptor agonist in the kidney
- NAME: N\-Nitro-L-arginine methyl ester, inhibitor of nitric oxide (NO) synthase
- DOCA: deoxycorticosterone, aldosterone precursor, sodium content and water retention in the kidney.

Data Analysis

- Four different treatments were applied in the study (Figure 2).
- The optimized protein expression for different hypertensive-induced treatments that may provide insight into underlying molecular mechanisms.
- To identify up regulated and down regulated proteins that lead to a diagnostic marker or a drug target.
- To discover markers for vascular remodeling that can be further confirmed through a targeted approach.

Results

Physiological Changes During Drug Treatments

- Figure 3 shows different murine models used in study, acute tissue samples collected at day 7, after first generation of the drug.

The following proteins were identified and validated:
- Angiotensin II: receptor agonist in the kidney
- NAME: N\-Nitro-L-arginine methyl ester, inhibitor of nitric oxide (NO) synthase
- DOCA: deoxycorticosterone, aldosterone precursor, sodium content and water retention in the kidney.

Summary and Future Directions

- Proteome expression levels of treated samples (Ang II, DOCA and NAME) are significantly different compared to the control group.
- DOCA-NAME models significantly differ in terms of number of protein IDs up- or down-regulated compared to other treatments.
- Some "proteins" are regulated independently of the treatment (fibronectin, hemopexin, and filamin).
- A list of up regulated targets will be selected based on these results as surrogate markers for further studies to quantify vascular remodeling under hypertension.

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