Targeting AhR metabolic circuitry for better diagnose and management of arterial hypertension

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Summary: (1000 characters)
The confluence of environmental exposure and polygenetic propensity are factors in essential arterial hypertension (HTN). Secondary HTN is associated to specific conditions such as obstructive sleep apnea (OSA). Despite the particularities of OSA-HTN, its treatment has been indistinguishable from essential HTN. A high prevalence of uncontrolled blood pressure is still found in OSA population even with concomitant use of continuous positive pressure and anti-hypertensive drugs.

Chronic intermittent hypoxia (CIH) is the endogenous exposure characteristic of OSA-HTN. We have been investigating how CIH triggers mechanisms of environmental adaption, namely xenobiotic-sensor aryl hydrocarbon receptor (AhR) and we found that AhR is particularly activated at the kidney when CIH-HTN is established.

We will investigate in animal model of CIH-HTN if abrogation of AhR-circuity will revert CIH-HTN and how CIH impacts endogenous AhR activators production, namely the kynurenine (Kyn) pathway. In parallel, Kyn pathway will be measured in control, HTN without OSA and HTN-OSA individuals in order to stratify patients as high or low activators of AhR metabolic circuitry. This information will identify patients at higher risk of failure to conventional anti-hypertensive therapy and new therapeutic targets for non-responsive patients.

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