Alteration of Renal Corticosteroid Signaling Pathways in Preterm Infants: Neonatal Adaptation and Developmental Programming of Hypertension

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Introduction
Prematurity, a worldwide health issue, is often associated with renal tubular immaturity leading to major salt losses, whose mechanisms remain poorly understood. Moreover, these premature infants are prone to develop hypertension early in adulthood, with several lines of evidences in favor of a phenotypic transmission to the offspring.

Objectives
To study the role of renal corticosteroid signaling pathways in the development of renal and cardio-vascular complications in preterm infants.

Clinical characteristics of preterm mice

Optimal model of preterm birth:
- Preterm neonates presented with maladaptation: Growth retardation, 70% of live births and 35% of long term survival.
- Significant early-onset hypertension in males.

Impact of prematurity on renal corticosteroid pathways

Strong activation of renal corticosteroid target gene transcription at birth in premature mice
Independently of MR and GR expression and plasma steroid levels
Not sustained in adulthood

Is there a dysregulation of blood pressure in the offspring?

Former preterm or control female mice
WT male mouse

F1
F2
F3

Genomic DNA
Specific amplification of Gilz promoter CpG island
Hypomethylation of the promoter region of Gilz
Strong correlation between methylation/expression of Gilz suggests an epigenetic regulation by DNA methylation

Conclusion:
We provide evidence for transgenerational dysregulation of blood pressure, induced by prematurity, associated with persistent increased expression of Gilz which could partly be in relation with an hypomethylation of its promoter.

- Better understanding of developmental programming of cardiovascular diseases
- Better management of premature infants from birth to adulthood

References