

# PHARMACOLOGICAL REGULATION OF CEREBROSPINAL FLUID

June Goto, PhD is a Research Instructor in the Department of Neurosurgery, Pediatric Division at Cincinnati Children's Hospital Medical Center. Dr. Goto combines genetic analysis with biological assays to determine the pathways involved with developmental abnormalities. In her study, *Molecular characterization and pre-clinical trial in a novel mouse model of congenital hydrocephalus*, Dr. Goto will analyze the link between a genetic mutation and very early onset fetal hydrocephalus in a new animal model.

## GOAL

Characterize new model for early onset congenital hydrocephalus

## RATIONALE

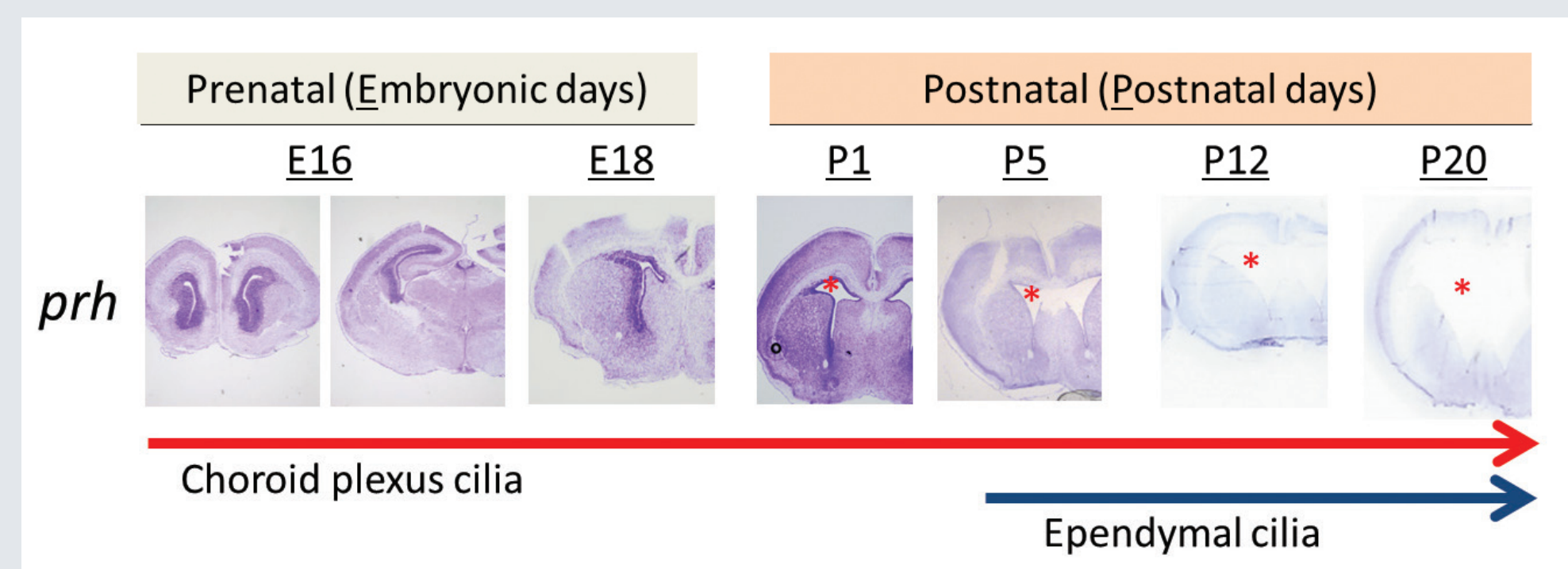
In many cases, the cause of congenital hydrocephalus is a mystery

New animal models can provide novel insights into how hydrocephalus develops

This can lead to better understanding of the condition and new drug targets

## NEW INSIGHTS WITH A NEW GENETIC MODEL

- 1 Ventricles enlarge very early in development (P1) (see visual)
- 2 A previous theory does not apply
- 3 A new theory emerges



## HOW DO WE UNRAVEL A NEW MODEL?

- 1 Find the Mutation: Sanger sequencing chromatograms for wt, parent, and prh. Mutations are circled: A/A in wt, A/T in parent, and T/T in prh.
- 2 Identify the Gene: Schematic of CCDC39 gene structure (Exon 6, Exon 7, Exon 8) and Western blot analysis. The prh mutation is a deletion of Exon 6 (22aa) and a truncation of Exon 7 (51aa\* & stop). The wt protein is 64aa.
- 3 Test Protein Levels: Western blot for CCDC39 and actin in Control and prh. The prh lane shows a significantly reduced CCDC39 band (circled in red).
- 4 Verify Expression Patterns: Immunofluorescence images for CCDC39/DAPI in wt and prh. In wt, CCDC39 is localized to the choroid plexus (CP). In prh, CCDC39 is absent from the CP (circled in red). Green indicates presence of protein.

## WHY IS THIS WORK INNOVATIVE?

The new animal model puts forward an alternative disease process. This may lead to new drug targets