How faulty vitamin A transport disrupts fetal eye development

Retinol, a form of vitamin A essential to eye development, is acquired from the diet and stored in the liver. Because retinol is not water-soluble, it must be transported through the bloodstream by a “carrier,” known as retinol binding protein (RBP4).

**In a normally functioning system,** cells that need or convey retinol for growth and development, such as the eye and placenta, have special STRA6 receptors on their cell membranes that act as portals, allowing the retinol/RBP4 complex to dock and release retinol into the cell.

**When RBP4 is mutated,** it cannot carry retinol from the liver, and to make matters worse, it also binds tightly to STRA6 receptors, blocking the portal and preventing retinol from entering the cell.

Researchers found that this molecular bottleneck produces its most devastating eye deformities when the RBP4 mutation is maternally inherited. In this case, retinol must be handed off twice – first, at the placenta, from the mother’s circulation to the fetal circulation, and then from the fetal bloodstream to the primordial eye. Paternal inheritance of the mutated gene allows sufficient retinol to pass through the placenta to support normal eye development.