SMCHD1 and Epigenetics: Lessons Learned from Patients Born Without a Nose

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SMCHD1 is a master epigenetic repressor that controls X-inactivation and silences a subset of autosomal genes. Loss-of-function and missense mutations in *SMCHD1* cause a late-onset degenerative muscle disorder called facioscapulohumeral muscular dystrophy, type 2 (FSHD2). In 2017, my group discovered that missense mutations in *SMCHD1* can also cause a completely different disorder - congenital arhinia (absent external nose) - a severe malformation that is often accompanied by ocular defects and hypogonadism. By conducting deep phenotyping studies in patients with arhinia or FSHD2 and performing functional studies in patient-derived embryonic cells, we are investigating the genetic and/or environmental modifiers responsible for these two divergent phenotypes.