Coffin-Lowry syndrome

Genetics

-RPS6KA3 (Ribosomal protein S6 kinase alpha-3)

-XLD; 70%-80% de novo; 20%-30% with >1 additional affected family member

Clinical findings/Dysmorphic features

-Severe to profound ID in males; males <3%ile in height; soft fleshy hands, tapering fingers with small terminal phalanges; microcephaly; kyphoscoliosis

-Stimulus induced drop episodes (SIDAs)

-Facial features in older males: prominent forehead/eyebrows, full supraorbital ridges, marked ocular hypertelorism, downslanting palpebrae, low nasal bridge, blunt tip, thick alae nasi and septum, large mouth, usually held open, patulous lips with everted lower lip, prominent ears

Etiology

-1:40,000 to 1:50,000

Pathogenesis

-Unclear; RPS6KA3 part of Ras signaling cascade --> cellular proliferation and differentiation

Genetic testing/diagnosis

-RPS6KA3 (35-40%), thereof 90-95% seq, 5-10% In/Del

Others

-Symptoms usually more severe in males than in females --> normal to profound ID in females