Computed tomography assesment in the characterization of mouse model for Costello Syndrome

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Purpose: Costello syndrome (CS) belongs to a group of neuro-cardio-facio-cutaneous (NCFC) developmental syndromes. Recently, it has been observed that NCFC syndromes result from *de novo* germ line mutations that alter the RAS/RAF/MEK signalling pathway. The malfunction in this pathway results in multiple clinical manifestations associated to NCFC syndromes such a developmental delay, musculoskeletal abnormalities and other physiological and neurological defects.

Methods: 4 adult mice (2 CS and 2 wild type) and 30 newborn P1 mice (15 CS and 15 wild type) were studied. The CT acquisition was performed using a CT system for small animal with an amperage of 200 uA and a voltage of 35 kV. Images were reconstructed using a modified FDK algorithm. To asses the morphological differences in adult and newborn mice, we collected a set of 12 two-dimensional landmarks in the midsagittal plane of the skull. Landmark configurations were aligned for translation and rotation by performing a Generalized Procrustes Analysis. **Results:** In the CT studies the H-*Ras*^{G12V} mutant mice display facial dysmorphia characterized by depressed anterior frontal bone, choanal atresia with shortened maxillary, molar process and premaxilar bone. Analysis of neonatal mice skull by CT scans revealed significant differences (Hotteling's T2 test; n=15) between CS and wild type mice in the landmarks of the anterior nasal area, nasal bone, center of alveolar ridge over maxillary incisor, and maxillar suture. **Conclusion:** These defects have a developmental origin since they can be already observed in neonatal mice. All together, these defects induce a quite prominent forehead and blunt nose that clearly distinguishes H-*Ras*^{G12V} mice from their wild type littermates