CFAO GRADUATE STUDENT POSTERBOARD ABSTRACTS

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Cell movements and tissue flow reshape the embryonic midface

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Objectives: Several syndromes and non-syndromic conditions include abnormal narrowing of the face with hypertelorism, broad nasal bridge and premaxillary hypoplasia. Our study investigated extrinsic versus intrinsic factors contributing to midline narrowing.

Methods: Frontonasal masses were dissected from stage 25 chicken embryos and a subset of cultures was treated with RhoGTPAse antagonist (ROCK) (10 µM Y27632). Organ cultures were photographed every 24h for 48h and the width between the nasal slits was measured. Other cultures were used for time-lapse confocal microscopy using Hoechst dye to visualize the nuclei.

Results: 3D analysis of the frontonasal mass revealed a significant increase in cranio-caudal height and dorsoventral depth at the same time as the medio-lateral axis is narrowing. We recapitulated these changes in vitro independent of whether the eyes, brain and even other facial prominences were attached to the frontonasal mass. This suggested that changes in shape were intrinsic to the facial prominences. We tested whether blocking cytoskeletal remodeling with ROCK antagonist would affect the narrowing. Treatment completely blocked narrowing in vitro and indicated that cell movements were required for midline narrowing. Time-lapse cell tracking of nuclei labeled with Hoechst stain within the cultured frontonasal masses showed that ROCK antagonist significantly reduces intrinsic movement of nuclei including convergence seen at 63X near the nasal slit.

Conclusions: We concluded that intrinsic cellular movement is a major mechanism underlying rapid tissue morphogenesis in the midface. Our novel live imaging methods allow direct observation of growing facial mesenchyme in normal and disease models.