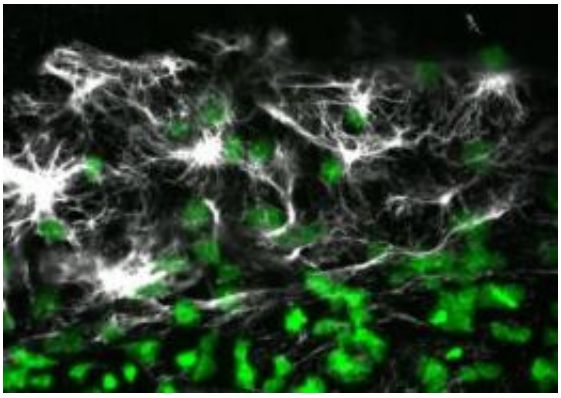
Bird embryo provides unique insights into development related to cancer, wound healing

March 23 2011, by Abby Robinson



This confocal image shows high levels of the protein vimentin (white) at the edge zone of a quail embryo. Cell nuclei are labeled green. Credit: Georgia Tech/Evan Zamir

(PhysOrg.com) -- Avian embryos could join the list of model organisms used to study a specific type of cell migration called epiboly, thanks to the results of a study published this month in the journal *Developmental Dynamics*. The new study provides insights into the mechanisms of epiboly, a developmental process involving mass movement of cells as a sheet, which is linked with medical conditions that include wound healing and cancer.

The study, published online on March 15, explains how epithelial cells expand as a sheet and migrate to engulf the entire avian egg yolk as it grows. It also reveals the presence of certain molecules during this

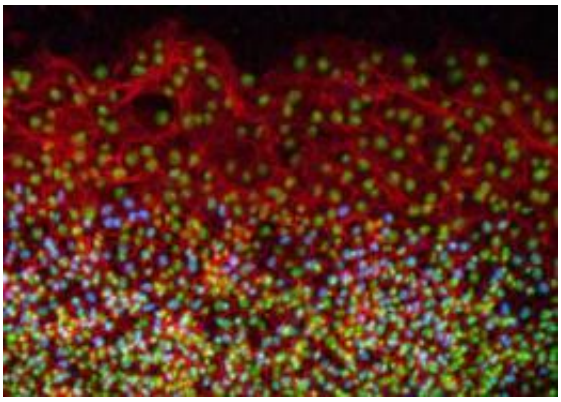
process that have not been previously reported in other major developmental models, including Xenopus frogs and zebrafish.

"These molecules and mechanisms of early development in the avian embryo may demonstrate evolutionary differences across species in the collective movement of epithelial cells and motivate additional studies of avian embryo development," said Evan Zamir, an assistant professor in the George W. Woodruff School of Mechanical Engineering at Georgia Tech.

Matt Futterman, who worked on the project as a graduate student at Georgia Tech, and mechanical engineering professor Andrés García also contributed to this study. The research was funded by Zamir's new faculty support from Georgia Tech and by a grant to García from the National Institutes of Health.

In the study, the researchers conducted immunofluorescence and high-resolution confocal microscopy experiments to examine the spatial distribution and expression of five proteins -- vimentin, cytokeratin, β-catenin, E-cadherin and laminin -- as cells moved to wrap the yolk sac of quail embryos during development.

The results showed that during this process, four of the proteins -- vimentin, cytokeratin, β-catenin and E-cadherin -- appeared in the cells located at the free edge of the migrating cell sheet. Finding dense interconnected networks of both vimentin and cytokeratin in the edge cells surprised the researchers.



This image shows that the edge zone (top of image) of the quail embryo shows no proliferating cells (cyan), unlike the interior zone (bottom of image). Non-proliferating cell nuclei are labeled green. Credit: Georgia Tech/Evan Zamir

"Since cytokeratin is generally associated with the epithelial phenotype and vimentin is generally associated with the mesenchymal phenotype, it's rare to see them expressed in the same cells, but this does occur in metastasizing tumor cells," said Zamir.

Cells expressing the mesenchymal phenotype are typically found in connective tissues -- such as bone, cartilage, and the lymphatic and circulatory systems -- whereas cells of the epithelial phenotype are found in cavities and glands and on surfaces throughout the body.

This finding provides evidence that epithelial cells normally attached to a membrane surface underwent biochemical changes that enabled them to assume a mesenchymal cell phenotype, which enhanced their migratory capacity. This process, called partial epithelial-to-mesenchymal transition, has many similarities to the initiation of tumor cell metastasis and wound healing.

Since this epithelial and mesenchymal expression pattern in the edge cells has not previously been reported in Xenopus or zebrafish, it may be

unique to the avian embryo. This discovery would make the avian embryo a valuable model for studying tumor cell migration and wound healing.

In addition to detailing protein expression in the quail embryo during development, the researchers also determined the origin of the new cells required at the migrating edge to cover the growing yolk. During development, the radius of the quail yolk doubles every day for the first few days, representing a hundreds-fold increase in the egg yolk surface area.

"For each individual cell that has to cover the egg yolk as it grows, the migration around the yolk is extraordinary, because it's such a large territory -- it'd be like an ant walking across the earth," explained Zamir.

Looking more closely at the edge cells, the researchers found strong evidence that expansion of the edge cell population was due exclusively to cells relocating from an interior region to the edge as the embryo expanded. The cells located at the free edge generated the bulk of the traction force necessary for expansion and towed the cells within the interior of the epithelium.

"These experiments confirm that edge cell proliferation is not the primary mechanism for expansion of the edge cell population," noted Zamir. "And our observation of epithelial-to-mesenchymal transition in the edge cells explains how these epithelial cells might be changing phenotype to become migratory in this rapidly expanding sheet."

To determine if this study's findings are indeed unique to the avian embryo, Zamir plans to conduct further studies to characterize protein expression and cell migration in Xenopus and zebrafish.