J Clin Exp Dermatol Res 2016, 7:4(Suppl)
http://dx.doi.org/10.4172/2155-9554.C1.030

Rapid RNAi and CRISPR based direct *in vivo* screening to systematically reveal novel squamous cell carcinoma genes

Daniel Schramek
University of Toronto, Canada

Mining the wealth of genomic data for personalized cancer therapies poses one of the biggest challenges for translational cancer research today and is predicated on weeding out 'bystander' mutation and identifying the 'driver' mutations and pathways responsible for initiating tumorigenesis and metastasis. We thus developed a novel RNAi methodology that allows us to simultaneously screen hundreds of putative human cancer genes directly *in vivo* using various mouse models of cancer. Importantly, this method tests gene function within the native tissue architecture, stromal cues and immune system. First, we focused on Head & Neck squamous cell carcinomas (HNSCCs), which represent the 6th most common cancer with a mortality >50%. Using ultrasound-guided in utero injections of lentiviral particles, we selectively delivered shRNAs to the single-layered surface ectoderm of living E9.5 mouse embryos, where stem cells stably incorporate and propagate the desired genetic alterations (RNAi) into adulthood in a mosaic fashion. This allowed us to identified seven novel tumor suppressors including Myh9, which encodes non-muscle myosin IIA. Mechanistically, we uncovered that myosin IIA's function is manifested not only in conventional actin-related processes but also in regulating p53 activation. Clinically, low Myh9 expression stratifies HNSCCs patients with poorest survival. We have now expanded our technology to various other epithelial cancer models, included CRISPR-mediated gene-editing and started with negative screening to elucidate physiological regulators of oncogenic growth further highlighting the utility of direct *in vivo* screening to integrate human cancer genomics and mouse modeling for rapid and systematic discovery of cancer driver mutations and novel cancer vulnerabilities.

schramek@lunenfeld.ca

Impact of antithrombin concentrate on healing of burnt skin: Preliminary results

Areta Kowal-Vern
Rush University Medical Center, USA

Antithrombin (AT) is a natural anticoagulant which has both anticoagulant and anti-inflammatory properties. After thermal injury, the body sustains a Systemic Inflammatory Response Syndrome (SIRS), which activates coagulation and fibrinolysis, resulting in subclinical disseminated intravascular coagulation (DIC). There is a depletion of the coagulation factors and an increase in fibrinolytic debris in the vasculature. In burn patients, who have been treated with human Antithrombin concentrate compared to controls who have not received AT concentrate, there has been a decrease in thromboses under the burnt skin and a resulting enhancement of the healing process. The role of skin pathology, cytokines, the coagulation system, shock proteins and CD markers is discussed.

akvern@comcast.net