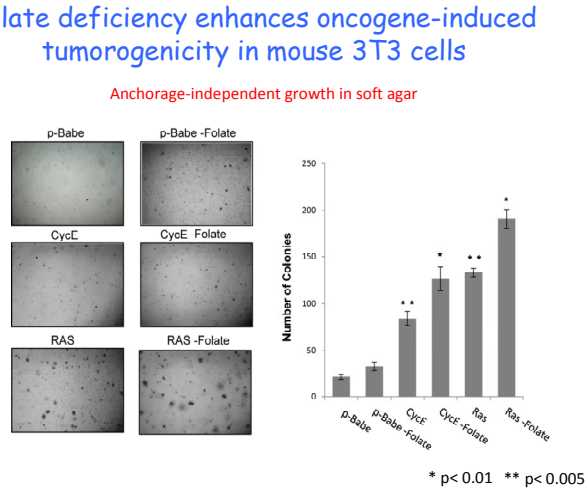
GUEST SPEAKER SEMINAR

Molecular Genetics
UNIVERSITY OF TORONTO

The molecular basis for replication-induced DNA damage in early stages of cancer development



Chromosomal instability is a hall mark of cancer. In early stages of cancer development the instability is caused by stress on the DNA replication. However, the molecular basis for this replication perturbation remained unknown. We have studied the replication dynamics in cells enforced to proliferate by aberrant activation of the Rb-E2F pathway. We found that oncogene expression enforces cell proliferation with an insufficient pool of nucleotides to support normal DNA replication resulting in replication perturbation, DNA damage and genome instability. An exogenous supply of nucleosides rescued the replication stress, decreased the replication-induced DNA damage and reduced transformation.
We further analyzed the effect of folate, an environmental factor essential for nucleotide biosynthesis, on early stages of cancer. We show that suboptimal levels of folate, which are associated with increased risk of cancer development, lead to concentration-dependent replication-induced DNA damage. Folate deficiency significantly enhances the replication stress caused by aberrant oncogene expression, leading to significantly increased DNA damage and tumorigenic potential.

Dr. Batsheva Kerem
The Hebrew University, Jerusalem

Host: Dr. Johanna Rommens

Date: Monday October 21, 2013
Time: 4:00 p.m.
Place: FitzGerald Building
150 College Street
Room 103