



BİLKENT UNIVERSITY
MOLECULAR BIOLOGY AND GENETICS
DEPARTMENTAL SEMINAR

"Age-dependent changes in KIT signaling and imatinib response oncogenic in a mouse model of gastrointestinal stromal tumor"

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Gastrointestinal stromal tumor (GIST) is the most common mesenchymal neoplasm of the human gastrointestinal tract. GISTs express KIT and they are thought to derive from a KIT⁺ or KIT^{low} interstitial cell of Cajal (ICC) progenitor or ICCs themselves. 69-89% of GIST lesions have a KIT activating mutation and 5%-13% of GIST lesions have a PDGFR α mutation. The most common activating mutations in GIST are found in *KIT* exon 11 which encodes the juxta-membrane domain of the KIT protein. A germline mutation of exon 11 found in a case of familial GIST had been introduced into the mouse *Kit* gene by a knock-in strategy in our lab before. The resulting *Kit*^{V558 Δ /+} mice develop cecal GIST with full penetrance. Imatinib mesylate is a tyrosine kinase inhibitor that inhibits KIT activity, and is used as a frontline treatment for advanced GIST patients. However, while *imatinib treatment* in GIST patients delays tumor progression, it does not cure the disease. We recently observed better histological response of GIST tumors to imatinib treatment in old *Kit*^{V558 Δ /+} mice compared to young mice. This is a surprising result since in general tumors are thought to become more aggressive over time. In this study we investigated whether key differences exist in signal transduction pathways in gastrointestinal stromal tumors from young mice versus old mice. We found that activation of ERK was diminished in old tumors and also activation of SRC and FAK was not further stimulated in old tumors upon imatinib treatment. These results highlight the importance of changes in ERK and SFK signaling during GIST progression.

Date-Time : Wednesday, December 16, 2015 – at 15:40

Place : SBZ-14

Host : Murat Cevher