

## 5<sup>th</sup> Asia-Pacific Summit on **Cancer Therapy**

July 20-22, 2015 Brisbane, Australia



### *Izhak Haviv*

Bar Ilan University, Israel

#### **Rational design of combination therapies and blockage of acquired targeted drug resistance**

Recent successes of targeted drugs on end stage cancer patients highlight the value of mutation-based biomarkers for drug response. However, the impact of these drugs is often temporary and the patients progress to acquired resistance. A common mechanism of drug evasion involves feedback mechanisms that increase expression or phosphorylation-driven activation of an alternative oncogenic pathway. The objective of this work was to set up a streamlined methodology (kinome profiling, shRNA negative RNAi screens, evolution tracking etc.) for rational drug combination designs. It includes pre-clinical assessment of the novel drugs focused on cancer cases, refractory to biomarker predicted targeting and seeking combination therapies that would block the spontaneous drug evasion. We explored the efficacy of the combination approach on a panel of cancer patient derived xenografts in mice using tumor size or metabolic imaging as an end point. Each cancer case was subject to target somatic mutation screening which resulted in a targeted drug recommendation and then mouse groups were treated either with sequencing-based therapy or with combination of these therapies with blockers of the suspected evasion mechanisms. As a blocker of the evasion mechanism and epithelial to mesenchymal transition, we characterized the utility of a molecule that leads to the destruction of IRS1/2 of the IGF1R pathway. Use targeted drugs such as Erlotinib, Zelboraf, Afinitorand Gleevec, all increase the attenuation of the cancer growth temporarily, followed by acquired resistance while inclusion of the IRS1/2 destruction lead to sustained efficacy and even lead to regression of the recurrent tumor mass.

#### **Biography**

Izhak Haviv has completed his PhD at the age of 32 years from Weizmann Institute of Science and Postdoctoral studies from University of California, Berkeley (c/o Tjian lab, Head, HHMI). He is the Director of cancer research center of excellence in the Faculty of Medicine in the Galilee of Bar Ilan University, an academic clinical and translational research organization. He has an Affiliate Position in the University of Melbourne for 11 years and at Peter MacCallum Cancer Centre, Australia for 16 years. He has published more than 59 papers in reputed journals.

[Izhak.Haviv@biu.ac.il](mailto:Izhak.Haviv@biu.ac.il)

#### **Notes:**