



### Targeting cancer stem cells: Challenges and opportunities

Xiaoyan Jiang

University of British Columbia, Canada

The introduction of molecularly targeted drugs in the 21<sup>st</sup> century marks a new and exciting era for cancer therapy. One of these new drugs is Imatinib (IM, Gleevec), a selective tyrosine kinase inhibitor that blocks the catalytic activity of the BCR-ABL oncoprotein. IM therapy has revolutionized the treatment of chronic myeloid leukemia (CML) worldwide. Nevertheless, early relapses and IM-resistant disease occur in a significant proportion of patients. Our recent studies indicate that CML stem cells are less responsive to IM and other tyrosine kinase inhibitors and are critical target population for IM resistance. Improved treatment approaches to prevent the development of resistant subclones by targeting other key molecular elements active in CML stem cells are thus clearly needed. One candidate is a complex we recently discovered that forms in CML stem/progenitor cells between the oncoproteins encoded by AHI-1 (Abelson helper integration site 1), BCR-ABL and the JAK2 kinase. This complex contributes to the transforming activity of BCR-ABL both *in vitro* and *in vivo* and also plays a critical role in the IM response/resistance of primary CML stem/progenitor cells. Interestingly, treatment with IM or dasatinib (DA) in combination with a new JAK2 inhibitor (TG101209) resulted in greater inhibition of CD34<sup>+</sup> CML stem/progenitor cells from IM nonresponders, compared to the same cells treated with a combination of IM and DA, as measured by colony-forming cell assays and long-term culture-initiating cell assays. These results suggest that targeting both BCR-ABL and JAK2 activities may be a potential therapeutic option for IM resistant patients.

#### Biography

Dr. Xiaoyan Jiang is a Senior Scientist in the Terry Fox Laboratory of the BC Cancer Agency, an Associate Professor in the Department of Medical Genetics and an Associate Member in the Department of Medicine at the University of British Columbia. She is also an Adjunct Professor at the Shanghai Institute of Medical Genetics of the Shanghai Jiao Tong University. She serves as an Editorial Board Member of 10 reputed journals, an external (ad hoc) reviewer for more than 20 journals and a research grant reviewer in Canada and the USA. She has published 45 peers-reviewed publications and 75 Abstracts.