Samir A. Farghaly, J Cell Sci Ther 2012, 3:7
http://dx.doi.org/10.4172/2157-7013.S1.004

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference on
Emerging Cell Therapies

October 1-3, 2012 DoubleTree by Hilton Chicago-North Shore, USA

Protein kinase braf inhibitors as targeted therapy for border line epithelial ovarian tumors

Samir A. Farghaly
The Weill Medical College of Cornell University, USA

Epithelial ovarian cancer patients can be broadly divided into 2 groups (type 1 and type 2 tumors) on the basis of histopathologic parameters. Type 1 tumors exhibit a shared lineage with the same distinct molecular signature in benign cystadenomas, borderline tumors, and low-grade serous carcinomas with mutations in the KRAS(Kirsten rat sarcoma virus) gene or its downstream mediator BRAF (V-RAF murine sarcoma viral oncogene homolog B1).More than half of the low grade serous tumorsharbor mutations of either BRAF or KRAS gene. Thefrequency of KRAS mutation is similar in mucinoustumors. Almost all of these tumors show a transition phasefrom benign lesion to the low grade carcinoma in regard toboth their histological and molecular spectrum.Borderline serous tumors and low grade invasive serouscarcinomas have some similarities in genomic alterations,but a lot of differences exist too. Some borderline tumorsnever progress, whereas some have the potential to become high grade. The protein kinase BRAF is a key component of the RAS-RAF signaling pathway which plays an important role in regulating cell proliferation, differentiation, and survival. Mutations in BRAF at codon 600 promote catalytic activity and are associated with 30% OF LOW-GRADE SERIOUS OVARIAN TUMORS. The BRAF gene encodes a RAF family protein, which isrecruited by active RAS to stimulate the MAP-kinasepathway. The location of the BRAF gene is on the shortarm of the chromosome 7 (7q34). Most of the mutations ofB-RAF are clustered in two regions. 90% of the mutationsoccurred within or adjacent to the activation segment inexon 15, which protects the substrate binding site. 92%of these are a single substitution of adenine (A) forthymidine (T) at nucleotide position 1796, which convertsa valine to a glutamic acid (Val to Glu) at positionexon 600 (V600E, formerly named V599E).Mutations were identified less commonly in the G loop(glycin rich loop), in exon 11, which mediates the bindingof ATP.The most common ovarian epithelial tumors are seroustumors and the second most common are mucinous tumors. More than have of these tumors, harbor mutations of either BRAF or KRAS gene. Thefrequency of KRAS mutation is similar in mucinoustumors. Almost all of these tumors show a transition phasefrom benign lesion to the low grade carcinoma in regard toboth their histological and molecular spectrum. Borderline serous tumors and low grade invasive serouscarcinomas have some similarities in genomic alterations.Dabrafenib has been identified as a potent ATP-competitive inhibitor of BRAF kinase and has been shown to be selective for mutant BRAF in kinase panel screening, cell lines, and xenografts. It has been shown to decrease tumor size by 28% in low grade ovarian tumors. The potential of this inhibitor as targeted therapy for low grade ovarian tumors will be discussed.

Biography

Samir A. Farghaly is a Physician/Scientist at the Weill Medical College of Cornell University, and the New York Presbyterian Hospital/ Cornell University Medical Center, New York, NY–USA. He received several national and international clinical and research awards. He has been an invited speaker in several national and international conferences on Women's health, Molecular genetic of female cancers, Gynecological cancer and Oncology. He is a member of several national and international societies, organizations, foundations of Women health and Cancer. He is an editor, member of editorial boards, editorial advisory boards and reviewers of several medical journals of Cancer Science & Therapy, Gynecology, Gynecological Cancer, Genomics, Clinical & Experimental Obstetrics and Gynecology, and Oncology. He has published 78 articles in reputed peer review journals. He has written several books chapters, and is an editor of (2) books on gynecological cancers, published in Feb. 2012, and the third book to be published in September 2012.

samirfarghaly@yahoo.com