

5th Asia-Pacific Summit on **Cancer Therapy**

July 20-22, 2015 Brisbane, Australia

Molecular analysis and clinicopathologic features of colorectal cancer from Algerian patients

K Berkane¹, H Benchaâ², S Ait Younes⁵, H Ait Kaci⁶, M Oukkal³, H Mahfouf⁴ and K Bouzid^{1,2}
Pierre & Mary Curie center, Algeria

Background: In Algeria, colorectal cancer (CRC) is the second most common cancer after lung cancer in men and breast cancer in women. The advances of molecular genetics using molecular markers MSI, BRAF and RAS mutations can predict prognosis and could contribute to decisions on treatment strategies. Determining the molecular profile of cancers offers the possibility of personalized treatment.

Material & Methods: We examined the clinico-pathological features and molecular profile of KRAS exon 2 codon 12 and 13, BRAF exon 15 codon 600 and MSI from 102 Algerian patients with advanced or m CRC.

Results: BRAF and KRAS mutations were detected in 4.9% and 31.3% of the patients' tumors respectively. Activating mutation in codon 12 and 13 in KRAS was located in the right colon 40.6% (13/32) vs. 25% (8/32) in the left colon ($p=0.130$) which tended to be more frequent at stage IV (55.8%) than at stage III (44.1%) ($p=0.960$). Approximately 64% (20/32) with KRAS mutation were well or moderately differentiated vs. 36% (12/32) ($p=0.130$). The poorly differentiated amino-acid changes are more frequently observed in codon 12 (20/32) than in codon 13 (3/32) and G12D is the most frequent mutation (14/32). The second is G12A (8/32) followed by G12V (3/32), G12C (2/32) and G13D (3/32). 18.6% (19/102) of the patients had MSI-H tumors and four of the tumors MSI-H had activating V600 E BRAF mutation.

Conclusion: Most of the clinico-pathologic characteristics observed in our study are similar to those reported in other studies and further analyses in larger series are required to confirm these preliminary results. Screening program should be set up to determine the incidence rate of the HNPCC which tend to be more frequent in Algeria than in western countries.

kenzaberkane05@yahoo.fr

Loss of HSulf-1 promotes defective autophagy and increased lipid droplet biogenesis in vitro and in vivo in ovarian cancer

Viji Shridhar¹, Debarshi Roy¹, Susmita Mondal¹, Ashwani Khurana¹, Xiaoping He¹, Edward Hammond² and Keith Dredge²

¹Mayo Clinic, USA

²Progen Pharmaceuticals, Australia

Dysregulation of autophagy and altered metabolic pathways are frequently observed in cancer. Due to these alterations, pharmacological targeting of these two pathways simultaneously could provide a viable therapeutic option. Although the association between these two pathways is well characterized in metabolic disorders, it is not well defined in ovarian cancer (OVCA). In this regard, we found that loss of endosulfatase HSulf-1, a known putative tumor suppressor suppresses LC3-GFP foci formation and promotes increased lipid droplet (LD) biogenesis suggesting that absence of HSulf-1 in OVCA affects both autophagy and lipid metabolism. While isogenic cells with genetic ablation of HSulf-1 (OV202Sh1/2 and TOV2223Sh1 cells) displayed LDs, the nontargeted control transduced (NTC) OV202 and TOV2223 cells had significantly less LDs. In contrast, Transmission Electron Micrographs (TEMs) showed that OV202 and TOV2223 NTC cells had significantly more autophagic vacuoles (AVs) compared to their isogenic ShRNA targeted cells. Conversely, ectopic expression of HSulf-1 in SKOV3 cells decreased the number of LDs and increased the number of AVs compared to vector transfected controls. Here we report that OV202Sh1 cells and HSulf-1 deficient OV2008 cells have increased p-cPLA2 α (ser505) levels that are associated with biogenesis of large number of LDs with reduced AVs. Interestingly, pharmacological inhibition of cPLA2 α with AACOCF3 in OV202Sh1 cells resulted in reduced LD biogenesis inhibited colony formation and reduced tumorigenesis in vivo. More importantly, treatment of HSulf-1 deficient cells with HS mimetic PG545 which can compensate for loss of HSulf-1, reduced LD biogenesis, promoted autophagy and inhibited tumor growth in vivo. Collectively, these results show a critical role of HSulf-1 in regulating both autophagy and LD biogenesis in ovarian cancer.

gaya03@gmail.com