J Cancer Sci Ther 2013, 5:10
http://dx.doi.org/10.4172/1948-5956.S1.030

OMICS Group Conferences
Accelerating Scientific Discovery

3rd World Congress on
Cancer Science & Therapy

October 21-23, 2013 DoubleTree by Hilton Hotel San Francisco Airport, CA, USA

Expression of a dominant negative HSP110 mutant by colorectal cancer cells decreases their survival and improves patient prognosis

Alex Duval
Saint-Antoine hospital, France

Heat shock proteins (HSPs) are necessary for cancer cell survival. We identified a mutated form of HSP110 (HSP110DE9) in colorectal cancer displaying microsatellite instability (MSI CRC), generated from an aberrantly spliced mRNA and lacking the HSP110 substrate binding domain. This mutant is expressed at variable levels in MSI CRC cell lines and primary tumors. HSP110DE9 impaired both the normal cellular localization of HSP110 and its interaction with other HSPs, thus abrogating the chaperone activity and anti-apoptotic function of HSP110 in a dominant negative manner. HSP110DE9 over expression caused the sensitization of cells to anticancer agents such as oxaliplatin and 5-fluorouracil which are routinely prescribed in the adjuvant treatment of CRC patients. The expression level of mutant HSP110 correlates with the size of allelic deletions in the *HSP110* T_{17} DNA repeat located in intron 8. We recently examined a consecutive, multicentre series of 329 patients with stage II or stage III CRC whose positive MSI status was prospectively identified at diagnosis using standardized methods. Both stage II and stage III CRC patients with large *HSP110* T_{17} deletions and who received adjuvant chemotherapy showed excellent relapse-free survival regardless of the regimen used. Multivariate models confirmed that the survival of stage III MSI CRC patients and of chemotherapy-treated MSI CRC patients was dependent on the mutation status of *HSP110* T_{17}. Mutations in *HSP110* T_{17} thus predict the outcome of patients with MSI CRC. The likely mechanism for this association is the chemosensitization of cancer cells following the loss of HSP110 chaperone function.

Biography

Alex Duval is M.D. and he has completed his Ph.D. at the age of 35 years from Paris René Descartes University and postdoctoral studies from French Institute of Health in the lab of Pr. Gilles Thomas in Paris. He is the director of the team 'Microsatellite Instability and Cancer', a research team whose activity is entirely dedicated to the study of MMR-deficient neoplasms. He has published more than 50 papers in reputed journals such as Nature Medecine, Journal of the National Cancer Institute, Journal of Clinical Oncology, Gut, Gastroenterology or PNAS.

Alex.Duval@inserm.fr

Benign prostate hyperplasia and prostate carcinogenesis after the chernobyl accident in Ukraine

Alina Romanenko[1], Sergey Vozianov[1], Vyacheslav Grygorenko[1], Anna Chekalova[1], Andriy Yurakh[1] and Pirkko Harkonen[2]
[1]Academy of Medical Sciences of Ukraine
[2]Lund University, Malmo, Sweden

During the 26-years period subsequent to the Chernobyl accident the morbidity of prostate cancer in Ukraine has increased from 12.0 to 28.6 per 100 000 of male population. The present study was conducted to evaluate the development of radiation-dependent lesions in benign prostate hyperplasia (BPH) patients living in cesium 137 (^{137}Cs) contaminated areas of Ukraine.

BPH samples were obtained by adenomectomy from 30 patients from so called clean (without radio-contamination) areas (control group 1) and 90 patients living in ^{137}Cs contaminated areas of Ukraine (group 2). These BPH samples were examined histologically and immunohistochemically (IHC). γ-H2AX, iNOS, Ki-67, p53, p63, p27Kip1 and Bcl-2 proteins were IHC investigated in BPH samples from all patients.

A pattern of chronic proliferative atypical prostatitis (CPAP) accompanied with large areas of sclerotic stromal connective tissue with increased angiogenesis, in association with dramatic increase in the incidences of areas of proliferative inflammatory atrophy (PIA), basal-cell hyperplasia (BCH) with cellular atypia as well as with the areas of prostatic intraepithelial neoplasia (PIN) were detected in group 2 BPH patients.

Our data support a strong relationship between long-term low-dose ^{137}Cs radiation exposure of BPH patients who lived about 26 years in radio contaminated areas and development of CPAP, a possible preneoplastic condition in humans. Our study suggests the alteration of cell cycle transition and apoptotic regulatory molecules in association with γ-H2AX and iNOS over expression at the areas of PIA and BCH with cellular atypia which could be also crucial early molecular events in the pathogenesis of the radiation induced prostate carcinogenesis.

romanenkoa5@hotmail.com