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Iodine-131 dose dependent gene expression in thyroid cancers and corresponding normal tissues following the Chernobyl accident

M. Abend

Bundeswehr Institute of Radiobiology, Germany

Abstract

We evaluated gene expression in thyroid tissue in relation to iodine-131 (I-131) doses received from the Chernobyl accident for studying radiation carcinogenesis in humans. Sixty three of 104 papillary thyroid cancers diagnosed between 1998 and 2008 in the Ukrainian-American cohort with individual I-131 thyroid dose estimates had paired RNA specimens from fresh frozen tumor (T) and normal (N) tissue provided by the Chernobyl Tissue Bank. We first hybridized 32 randomly allocated RNA specimen pairs (T/N) on 64 whole genome microarrays (Agilent, 4x44K). Associations of differential gene expression ($\log_2$(T/N)) with dose were assessed using Kruskal-Wallis and trend tests in linear mixed regression models. We selected 75 genes with *a priori* evidence or P kruskal/P trend < 0.0005 for validation by qRT-PCR on the remaining 31 RNA specimen pairs (T/N). The qRT-PCR data were analyzed using linear mixed regression models that included radiation dose as a categorical or ordinal variable. Eleven of 75 qRT-PCR assayed genes (*ACVR2A*, *AJAP1*, *CA12*, *CDK12*, *FAM38A*, *GALNT7*, *LMO3*, *MTA1*, *SLC19A1*, *SLC43A3*, *ZNF493*) were confirmed to have a statistically significant differential dose-expression relationship. A second approach followed, but this time we examined for gene expression separately in the tumor as well as the normal tissue. Results will be presented during this meeting. Our study is among the first to provide direct human data on long term gene expression in relation to individual I-131 doses and to identify a set of genes potentially important in radiation carcinogenesis.

Biography

Dr. Abendis employed as a Deputy Director at Bundeswehr Institute of Radiobiology affiliated to University Ulm, Germany. He earned a doctor degree in Medicine, a professorship in Radiobiology and a Master of Science in Epidemiology. His current research interest includes long lasting modifications of gene expression in response to ionizing radiation. To gain insight into this research he joins international collaborations merging divergent fields such as molecular biology, medicine, biostatistics and radioepidemiology.