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Evaluation of clonal origin of malignant mesothelioma

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The hypothesis that most cancers are of monoclonal origin is often accepted as a fact in the scientific community. This dogma arose decades ago, primarily from the study of hematopoietic malignancies and sarcomas, which originate as monoclonal tumors. The possible clonal origin of malignant mesothelioma (MM) has not been investigated. Asbestos inhalation induces a chronic inflammatory response at sites of fiber deposition that may lead to malignant transformation after 30-50 years latency. As many mesothelial cells are simultaneously exposed to asbestos fibers and to asbestos-induced inflammation, it may be possible that more than one cell undergoes malignant transformation during the process that gives rise to MM, and result in a polyclonal malignancy. To investigate the clonality patterns of MM, we used the HUMARA (Human Androgen Receptor) assay to examine 16 biopsies from 14 women MM patients. Out of 16 samples, one was non-informative due to skewed Lyonization in its normal adjacent tissue. Fourteen out of the 15 informative samples revealed two electrophoretically distinct methylated HUMARA alleles, the Corrected Allele Ratio (CR) calculated on the allele peak areas indicating polyclonal origin MM. Our results show that MM originate as polyclonal tumors and suggest that the carcinogenic "field effect" of mineral fibers leads to several premalignant clones that give rise to these polyclonal malignancies.

Biography

Sabahattin Comertpay has completed his PhD from University of Hawaii at Manoa, USA and is currently doing his Postdoctoral work at Middle East Technical University. He has published six papers some of which were published in high-impact journals, such as Nature Genetics and PNAS. He was recently by Scientific and Technological Research Council of Turkey for a project to investigate the apoptotic effects of capsaicin on malignant mesothelioma cell cultures.

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