Cancer from asbestos caused by more than one cell mutation

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It has been a long held belief that tumors arising from exposure to asbestos are caused by mutations in one cell, which then produces multiple clones. This hypothesis is challenged by new research published in the open access *Journal of Translational Medicine*, which suggests it is caused by mutations in multiple cells.

Malignant mesothelioma is a rare form of cancer that affects the mesothelium - the protective lining that covers the internal organs, such as the lungs, the heart and the abdominal cavity. It is estimated that malignant mesothelioma affects up to 3,200 people in the USA each year, most of whom die within a year of diagnosis. The primary cause of this cancer is exposure to asbestos, which used to be used in building construction. The inhalation of asbestos fibers causes inflammation that can cause mutations in cells even after 30-50 years of dormancy.

Most cancers are thought to be monoclonal, where all the cells in a tumor can be traced back to a mutation in a single cell. Researchers from University of Hawaii Cancer Center set out to investigate whether this was the case with malignant mesothelioma, or if it was polyclonal in which the tumor is the result of the growth of two or more mutant distinct cells.

During early development of the female embryo one of the two X chromosomes becomes inactivated and this inactivation is passed on to all subsequent cells. By tracing this inactivated X using a process called HUMARA assay it is possible to determine whether or not a cancer is monoclonal.

In this study, 16 samples from 14 tumor biopsies from women with mesothelioma had a HUMARA assay performed on them. These were compared to control DNA samples from a healthy male and female, and a known monoclonal cell line. The samples provided insight into the origin of the tumors and they were found to be polyclonal.

Lead researcher, Michele Carbone from University of Hawaii, says: "Our study indicates that malignant mesothelioma is the result of polyclonal tumors, a finding that has implications for our understanding of the disease and the clinic. For example, patients that have their tumors removed at the early stages of this type of cancer will most often go on to have a recurrence in spite of the appearance of the eradication of malignant mesothelioma. This new insight helps us understand why that may be."

These findings have implications for future research, especially with the advent of genomic medicine in the treatment of tumors. These results suggest that future approaches should target polyclonal cancerous cells with different types of mutations rather than a single monoclonal cell.

Michele Carbone says: "Our findings underscore the need to attack simultaneously several different molecular targets to try to eliminate the different malignant mesothelioma cell clones, as each clone may carry its own distinct set of molecular alterations."

More information: Evaluation of Clonal Origin of Malignant Mesothelioma , Sabahattin Comertpay, Sandra Pastorino, Mika Tanji, Rosanna Mezzapelle, Oriana Strianese, Andrea Napolitano, Francine Baumann, Tracey Weigel, Joseph Friedberd, Paul Sugarbaker, Thomas Kruasz, Ena Wang, Amy Powers, Giovanni Gaudino, Shreya Kanodia, Harvey Pass, Barbara Parsons, Haining Yang and Michele Carbone , *Journal of Translational Medicine* 2014, 12:301 www.translational-medicine.com/content/12/1/301

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