

PRESS RELEASE

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Preston M. Moretz

Epigenetic activity silences Rb2/p130 gene in lung cancer and retinoblastoma cells "Simple test could be developed to determine cancerous or pre-cancerous conditions".

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The attaching of methyl--or chemical--groups onto DNA sequences within the tumor suppressing gene Rb2/p130 can cause the gene to cease functioning in non-small lung cancer cells (NSLC) and retinoblastoma cells, researchers at Temple University's Sbarro Institute for Cancer Research and Molecular Medicine and Italy's University of Siena have discovered.

Their findings are reported in two studies: "Tumor-specific exon 1 mutations could be the 'hit event' predisposing Rb2/p130 gene to epigenetic silencing in lung cancer" and "Genetic and epigenetic alterations of RB2/p130 tumor suppressor gene in human sporadic retinoblastoma: implications for pathogenesis and therapeutic approach," both of which appear in September issues of *Oncogene* (<http://www.nature.com/onc>).

The joint studies at Temple and Siena were coordinated by Antonio Giordano, M.D., Ph.D., director of Sbarro Institute at Temple (<http://www.shro.org>), and by Marcella Macaluso of the Sbarro Institute and Caterina Cinti of both Centro Nazionale Ricerche and the University of Siena.

Giordano said that the researchers were puzzled when they found Rb2/p130, the tumor suppressing gene discovered by Giordano in the early 1990s, in an epigenetic state in both the NSLC and retinoblastoma cells. In this epigenetic state, the gene showed no signs of mutation, but is silent in its expression or function.

Further examination of the gene found that it had been methylated, a process in which methyl or chemical groups attached themselves to the gene, attacking a sequence of the Rb2/p130's DNA and thus causing it to cease functioning.

"These studies are providing very important information on how cancerous and pre-cancerous conditions can be detected by the presence of the methylated state of Rb2/p130." said Giordano. "These cancerous or pre-cancerous conditions can be treated with drugs or agents that de-methylate the Rb2/p130 gene. Once the drugs or agents disconnect the methyl groups from Rb2/p130, the gene begins to again express itself or function normally."



He likened this methylation/de-methylation phenomenon--which can stop or start the expression of a gene--to a lightswitch which is used to turn a lamp off or on. Giordano said some of these agents that will de-methylate Rb2 are already available, but have not been previously used because researchers did not know that the lack of expression from the gene was being caused by its methylation.

"Our discovery is providing a smart method to identify novel methylated drugs or agents that can assist in restarting the vital expression of Rb2/p130." he said.

Through the use of a simple genetic (both at DNA and Protein level) test of Rb2 gene and protein from a human tissue sample, said Giordano, scientists could determine if cancerous or pre-cancerous conditions exist because of the epigenetic state of the gene.

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"We could develop a potential test which could save many, many people from the ravages of cancer." he said.

NOTE: Copies of these studies are available to working journalists and may be obtained by contacting Preston M. Moretz in Temple University's Office of Communications, 215/204-7476 or pmoretz@temple.edu.