MedicalXpress

Why chemo works for some people and not others

September 18 2008

MIT researchers have shown that cells from different people don't all react the same way when exposed to the same DNA-damaging agent — a finding that could help clinicians predict how patients will respond to chemotherapy.

The research team from MIT's Center for Environmental Health Sciences (CEHS) and the Departments of Biological Engineering and Biology, identified a group of 48 genes that can predict how susceptible an individual is to the toxic compound, known as MNNG. The work appears in the Sept. 19 online edition of *Genes and Development.*

MNNG, a DNA-damaging compound similar to toxic chemicals found in tobacco smoke and in common chemotherapy agents, usually kills cells by inducing irreparable DNA damage. However, the researchers found a wide range of susceptibility among cells taken from healthy people.

"A cell line from one person would be killed dramatically, while that from another person was resistant to exposure," said Rebecca Fry, former MIT research scientist and lead author of the paper. "It wasn't known that cell lines from different people could have such dramatic differences in responses."

Toxic agents such as MNNG create lesions in DNA, provoking the cell to defend itself with a variety of DNA-repair and other pathways. However, every individual expresses slight differences in the genes

involved in those pathways.

"Even if everyone is exposed to exactly the same things, they would respond differently, because we're all genetically different," said Leona Samson, senior author of the paper, director of CEHS, and an American Cancer Society Research Professor.

The team members found that after measuring the expression of every gene in each cell line, they could predict cell sensitivity to MNNG from the expression of just 48 specific genes, with 94 percent accuracy.

Several of those 48 genes have already been linked to cancer, said Samson, but it was not known that their expression is already altered before exposure to the DNA damaging agent.

Source: Massachusetts Institute of Technology