MedicalXpress

A new mouse could help understand how some lung cancer cells evade drug treatment

December 9 2009

Lung cancer is the leading cause of cancer mortality worldwide and lung adenocarcinoma is the most common type. Many cases of lung adenocarcinoma are attributed to a mutation in a gene for the epidermal growth factor receptor (EGFR). Lung cancer with changes in EGFR is initially treatable with a family of chemotherapeutic agents called tyrosine kinase inhibitors (TKIs), such as gefitinib and erlotinib. However, patients often develop resistance to these drugs through the acquisition of additional changes or secondary mutations that allow cancer cells to evade treatment.

Some secondary mutations to the EGFR gene that allow lung cancer cells to survive in the presence of current chemotherapy are known. These secondary changes are now the focus of targeted efforts to create drugs to specifically interfere with the mutated form of the protein. Unfortunately, in 40% of the cases in which patients become resistant to therapy, the molecular events that confer this resistance are not known. Without knowing the changes that sustain the survival of these cells it remains impossible to specifically and effectively target them with anti-cancer drugs.

Scientists now describe a mouse model of lung cancer that develops resistance to TKI drugs in at least some of the same ways that humans do. Lung cancer occurs in these mice due to a mutation in EGFR that is the same as the mutation that underlies many human lung adenocarcinomas. Some of the defined secondary changes to EGFR, which are known to confer drug resistance in humans, also occur in these

mice. But most of these drug resistant mice bear tumors that do not contain known mutations. This important similarity to the human situation suggests that this mouse model might help identify the currently unknown mutations that make lung cancer cells resistant to therapy.

Many techniques are now available to unravel the genetic changes that occur in cancer cells. Since these mice recapitulate many of the known mutations that characterize human lung cancer, the hope is that their cells can be screened to identify the currently unknown mutations that promote drug resistance in lung cancer cells. This provides a model to uncover the molecular events responsible for the 40% of patients that become resistant to TKI therapy due to unknown causes. Once novel mechanisms of resistance are identified, these mice might also become valuable preclinical systems to evaluate the efficacy of therapeutics developed to combat drug-resistant disease.

Source: The Company of Biologists (news : web)