

Scientists clarify molecular basis of interferon action

Scientists at the University of California, Santa Barbara have made a significant discovery relating to viral infections in humans.

They studied how a certain enzyme called PKR behaves in human cells, and showed that this enzyme is important for the antiviral effect of interferon against some viruses, but not others. Interferon is a naturally occurring substance that is also used as a drug to treat certain viruses such as Hepatitis C.

The findings will be published in the *Journal of Virology* in August (Volume 81, issue 15), and the article is currently available on-line at <http://jvi.asm.org/cgi/reprint/JVI.00426-07v1?view=long&pmid=1752227>.

The study was conducted in the laboratory of Charles Samuel, the Charles A. Storke II Professor of Molecular Biology at UCSB. The first author is Ping Zhang, a postdoctoral fellow.

The overall objective of Samuel's laboratory is to elucidate, in molecular terms, the mechanisms by which interferons exert their antiviral and cell growth control actions in mammalian cells.

“The interferon system is an important host defense against viral and microbial pathogens,” said Samuel. “In addition to inhibiting virus multiplication, interferons affect other processes in animal cells, including cell growth and differentiation and the immune response.”

Current work in Samuel's lab includes biochemical and molecular genetic studies of two interferon-inducible enzymes, PKR and ADAR. The new study deals with the enzyme PKR, an RNA-dependent protein kinase. (RNA stands for ribonucleic acid and is a type of enzyme that is involved in phosphorylation, the transfer of phosphates from donor molecules to target molecules.)

The researchers cultured human cancer derived cells with very low PKR — or none at all. This allowed them to test the role of PKR in the cell.

“We found that with low PKR there is less apoptosis in response to some stimuli,” said Zhang. (Apoptosis is cell death or “suicide.” It is a strategy, at the cellular level, to prevent growth of the virus.)

The scientists found that protein synthesis, including the synthesis of an invading virus, is also affected by PKR.

Using three separate viruses, the scientists found that PKR is important for the antiviral effect of interferon against some viruses but not others.

The current study extends findings from studies of mouse cells that are genetically deficient in PKR. It clarifies certain roles of PKR in apoptosis, signaling, and virus replication in a human cell.

Source: University of California - Santa Barbara

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