URLs

Entrez Gene:

<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=genome>

JCV

<http://www.ncbi.nlm.nih.gov/genomes/framk.cgi?db=genome&gi=10684>

Swiss-Prot:

<http://www.expasy.ch/>

Agno

<http://us.expasy.org/cgi-bin/niceprot.pl?P03086>

HP1 α

<http://us.expasy.org/cgi-bin/niceprot.pl?P45973>

LBR

<http://us.expasy.org/cgi-bin/niceprot.pl?Q14739>

VIRAL INFECTION

Agno finds a way out

A recent study in *EMBO Reports* has shed light on the mechanism used by a human polyomavirus, the JC virus (JCV), to export viral particles from the host cell nucleus.

The progeny of JCV — the causative agent of progressive multifocal leukoencephalopathy (PML) — are packaged inside the nucleus of infected cells, and the surrounding nuclear envelope therefore presents a barrier that must be overcome for efficient nuclear egress. One way for the virus to bypass this obstacle is, of course, to lyse the nuclear envelope. However, by preserving the integrity of the nucleus, viral replication can continue uninterrupted, a strategy that is used by JCV to optimize intercellular spread.

So, how do JCV virions escape into the cytoplasm? To answer this question, Hirofumi Sawa and colleagues focused on the JCV late gene product, the agnoprotein (Agno), as its perinuclear localization in infected cells hinted at a role in nuclear transport.

The authors characterized the binding partners of Agno and, interestingly, the heterochromatin protein-1 α (HP1 α) was found to interact with the N terminus of Agno.

HP1 α is a nuclear protein that associates with chromatin and binds promiscuously through a region known as the chromoshadow domain. One of its known protein partners is lamin-B receptor (LBR), an integral inner-nuclear-membrane protein, and it is thought that the binding of HP1 α both to chromatin and to LBR

stabilizes the nuclear envelope. So, the authors proposed that the binding of HP1 α to Agno might disrupt the HP1 α –LBR interaction, thereby altering nuclear envelope structure. By generating a cell line that expressed Agno on induction (293AG cells), the researchers could show that this was indeed the case — HP1 α interacted with Agno at the expense of its interaction with LBR. Also, fluorescence recovery after photobleaching (FRAP) analysis revealed that, under conditions of high Agno expression, LBR was less constrained in the nuclear membrane of these cells.

Finally, Sawa and his team microinjected virion-like particles into the nucleus of 293AG cells, and showed that these particles efficiently exited the nucleus only when Agno was expressed. As the JCV Agno N terminus shows high homology to the N termini of other polyomavirus agnoproteins, it is likely that the translocation of virions out of the nucleus is a conserved function of these proteins.

Shannon Amoils

References and links

ORIGINAL RESEARCH PAPER Okada, Y. & Suzuki, T. *et al.* Dissociation of heterochromatin protein 1 from lamin B receptor induced by human polyomavirus agnoprotein: role in nuclear egress of viral particles. *EMBO Rep.* **6**, 29 Apr 2005 (doi:10.1038/sj.embor.7400406)

WEBSITE

Hirofumi Sawa's laboratory: <http://www.hokudai.ac.jp/veteri/coe/e/Zoonosis/index.html>

Schematic showing the nuclear export of microinjected virion-like particles (VLPs) after induction of Agno expression. Figure courtesy of H. Sawa, Hokkaido University, Sapporo, Japan.