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Friend or foe? Antiviral molecule kills liver cells during hepatitis

Viral hepatitis is a global health threat: More than five hundred million people worldwide are infected with Hepatitis B and C viruses. The pathogens have a detrimental effect on the liver, which manifests with a complex pathology that is largely unknown. In their most recent study, published in "*Immunity*", CeMM researchers shed light on how this damage develops.

This study, which is the result of an international collaborative network led by Andreas Bergthaler (*http://www.cemm.oeaw.ac.at/research/groups/andreas-bergthaler-group/*) at CeMM, describes a surprising finding: Interferon, a defense protein against infections, which was thought to have mainly a protective function, contributes to the development of liver damage.

A two-faced molecule

After binding to its receptor on the surface of liver cells, interferon induces a signal that downregulates an enzyme (SOD1) which is responsible for cleaning up dangerous free radicals within the cell. As a consequence, these free radicals called "reactive oxygen species" (ROS) accumulate, destroy the cellular structures and ultimately kill the cell.

Bergthaler and his colleagues were the first to discover this harmful effect of interferon, although this cytokine has been studied since the 1960s. "This shows how complex and diverse the functions of interferon are", Bergthaler explains. So far he can only speculate, why the otherwise protective molecule is acting noxious in viral hepatitis.

Interferon blockade prevents tissue damage

Not only did the researchers discover the molecular principle behind the development of the interferon-driven liver damage – they even managed to prevent it in their models. By applying an antibody which binds the interferon receptor, they were able to avoid the accumulation of free radicals and protect the cells against oxidative damage.

Interferon is involved in a broad spectrum of infections. Thus, these newly discovered mechanisms may not only bear the potential to better understand hepatitis but many other diseases as well. They could also contribute to improve existing interferon-based therapies of non-infectious diseases like multiple sclerosis and cancer. "This basic research poses several new exciting questions", Andreas Bergthaler emphasizes. "At the same time it provides a novel paradigm for how interferon and free radicals cause infection-associated tissue damage".

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You can find a **short explanatory video** following this link: https://vimeo.com/145846544.

Publication:

Superoxide Dismutase 1 Protects Hepatocytes from Type I Interferon-Driven Oxidative Damage
Anannya Bhattacharya*, Ahmed N. Hegazy*, Nikolaus Deigendesch, Lindsay Kosack, Jovana Cupovic, Richard K. Kandasamy, Andrea Hildebrandt, Doron Merkler, Anja A. Kühl, Bojan Vilagos, Christopher Schliehe, Isabel Panse, Kseniya Khamina, Hatoon Baazim, Isabelle Arnold, Lukas Flatz, Haifeng C. Xu, Philipp A. Lang, Alan Aderem, Akinori Takaoka, Giulio Superti-Furga, Jacques Colinge, Burkhard Ludewig, Max Löhning**, Andreas Bergthaler**. Immunity, November 17 2015
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Funding:

CeMM gratefully acknowledges funding from the Austrian Academy of Sciences (ÖAW), the European Research Council (ERC Advanced Grant i-FIVE), the Austrian Science Foundation (FWF, Stand-alone project P23991), The European Molecular Biology Organisation (EMBO) and the German Academic Exchange Service (DAAD).

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