

Identification of a novel tumor suppressor

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CD4/CD8 double positive T-cell lymphoma cells (upper right quadrant) in lymph node

(PhysOrg.com) -- Scientists from the Friedrich Miescher Institute for Biomedical Research (FMI), have identified a novel tumor suppressor playing an important role in T-cell lymphoma. The protein kinase NDR1 has so far been implicated in the processes controlling cell death and centrosome duplication. In a recent study published in Science Signaling the FMI scientists show that T-cell lymphomas develop once the protein NDR1 is lost.

FMI Postdoc Hauke Cornils is excited: "We have found a novel tumor suppressive function for NDR kinases, which seem to play an important role in T-cell lymphoma not only in mice but also in humans." His excitement is understandable because tumor suppressors inhibit cancer development by multiple mechanisms such as restricting <u>cellular</u>



proliferation or promoting cell death. Loss of <u>tumor suppressor</u> function is therefore directly linked to <u>cancer development</u>. The identification of a novel tumor suppressor is always a good starting point to understand better the molecular mechanisms leading to cancer.

The kinase NDR1 has been known to regulate cell death in cell culture systems. To study the role of NDR1 in <u>cell death</u> regulation in vivo, FMI scientists around Hauke Cornils and Brian A. Hemmings, the group leader leading the kinase efforts at the Friedrich Miescher Institute for Biomedical Research, analyzed mice lacking NDR1. To their surprise they found that NDR1's sister kinase called NDR2 often chips in functionally and takes on some of the NDR1 tasks. Next, the scientists could show that a reduction in the amount of both NDR1 and NDR2 protein leads to the development of T-cell lymphomas in mice. "The upregulation of NDR2 in NDR1 deficient mice seems to be a protective mechanism against tumor development," says Hauke Cornils, "We were happy to observe that in tumors both kinases were indeed downregulated." What's more, when the FMI scientists together with their colleagues from the Institute of Pathology at the University of Basel analyzed T-cell lymphoma samples from patients, they found that NDR kinase protein levels were reduced in these samples as well. This strongly supports the notion that NDR kinases function as a tumor suppressor is conserved between humans and mice.

"We do not know yet, how exactly NDR kinases are down regulated in Tcell lymphoma. But we believe we have found a potential cellular marker for progression into T-cell lymphoma," explains Hauke Cornils. Reduced levels of NDR proteins could therefore be used as a diagnostic marker for T-cell lymphoma. "We would now like to look into other tumors as well. May as well be, that we have found a tumor suppressor that controls entry into a variety of cancers."

More information: Paper: stke.sciencemag.org/cgi/conten ...



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Provided by Friedrich Miescher Institute for Biomedical Research

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