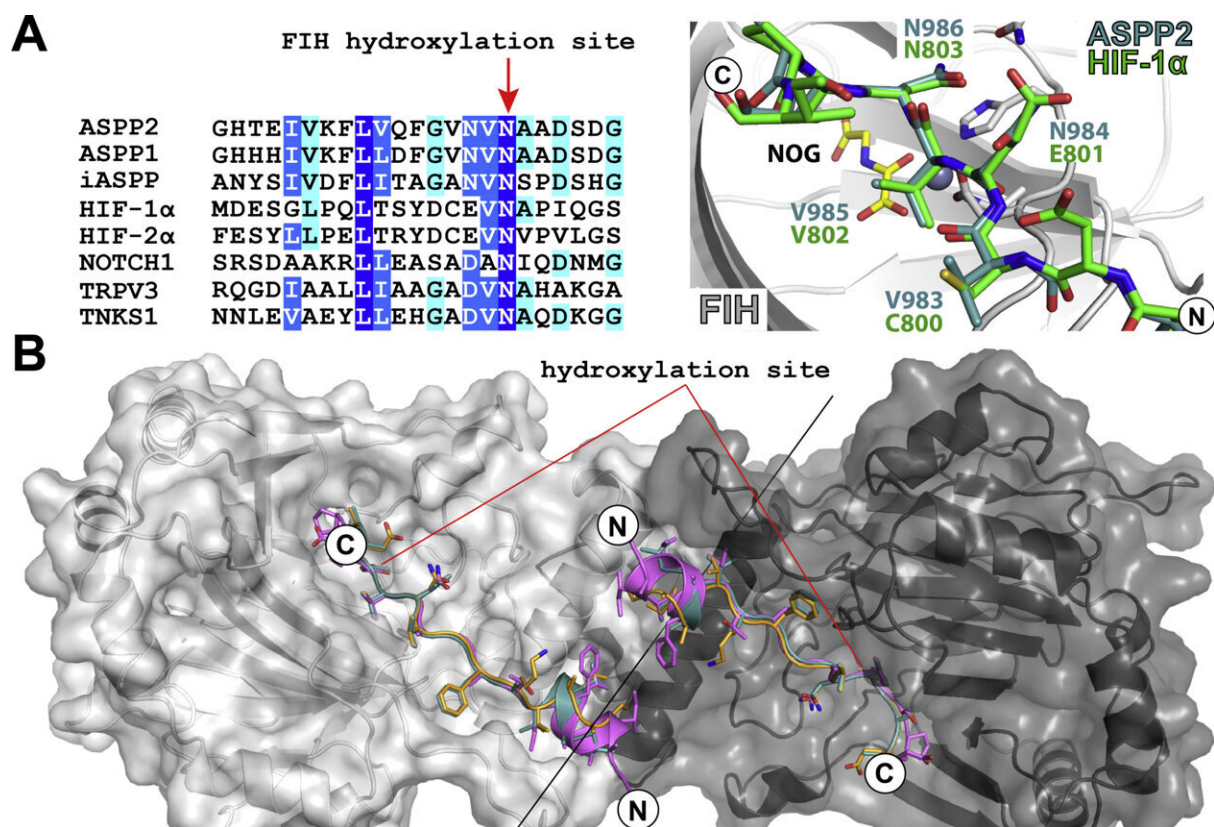


The hydroxylation of ASPP2 and other ankyrin repeat domain proteins

May 24 2022



Views from crystal structures of FIH in complex with ASPP derived peptides. A (Left) Sequence alignment of ASPP proteins with reported FIH substrates. (Right) Overlay of crystal structure derived views of FIH in complex with ASPP2 and HIF-1 α (PDB code 1H2K, 2.15 Å) showing the conserved nature of substrate binding. B Views from the dimeric structure of FIH in complex with an iASPP derived peptide (residues 670-693), an ASPP1 derived peptide (residue 932-954) and an ASPP2 derived peptide (residue 969-991). C Close up views from crystal structures of FIH in complex with ASPP derived peptides, the Fo-

Fc OMIT maps, shown in green mesh, are contoured to 3σ . Credit: *Journal of Biological Chemistry* (2022). DOI: 10.1016/j.jbc.2022.102020

Factor Inhibiting Hypoxia Inducible Factor (FIH) has an important role in the response to low oxygen (hypoxia) in animals. FIH adds a hydroxyl (-OH) group onto the master regulator Hypoxia Inducible Factor (HIF), influencing its ability to activate hundreds of genes that mediate the body's response to hypoxia. It also hydroxylates members of the ankyrin repeat domain protein family, including adding a single hydroxyl group to ASPP2 on asparagine 986.

ASPP2 is involved in several aspects of cancer biology, including the regulation of cell polarity/adhesion and the transcriptional activity of the tumor suppressor protein p53. However, the effect of hydroxylation by FIH on ASPP2's activity is still unclear.

A study led by former Ludwig Oxford researcher Thomas Leissing and his Oxford colleague Christopher Schofield, conducted in collaboration with the labs of Ludwig Oxford Director Xin Lu and Ludwig Member Peter Ratcliffe, investigated the hydroxylation of ASPP2 and other ankyrin repeat domain proteins.

Unexpectedly, in addition to the known site of hydroxylation, the team uncovered the ability of FIH to add [hydroxyl groups](#) to both asparagine residues within the "VNVN" motif present in ASPP proteins. Further characterization confirmed this to be a new type of post-translational hydroxylation.

Future work will define the role of this unprecedented modification by FIH in ankyrin repeat domain protein biology and in the response to [hypoxia](#).

This research is published in the *Journal of Biological Chemistry*.

More information: Thomas M. Leissing et al, Factor inhibiting HIF can catalyse two asparaginylation-hydroxylations in VNVN motifs of ankyrin fold proteins, *Journal of Biological Chemistry* (2022). [DOI: 10.1016/j.jbc.2022.102020](https://doi.org/10.1016/j.jbc.2022.102020)

Provided by Ludwig Cancer Research

Citation: The hydroxylation of ASPP2 and other ankyrin repeat domain proteins (2022, May 24) retrieved 26 April 2024 from <https://phys.org/news/2022-05-hydroxylation-aspp2-ankyrin-domain-proteins.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.