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*Hypothesis*

# Ring finger in the peroxisome assembly factor-1

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The peroxisome assembly factor-1 (PAF-1) is reported here to contain the signature subsequence for a ring finger motif in its carboxyl-terminus. This conserved subsequence in PAF-1 may be the key to a gene expression regulatory pathway important in peroxisome biogenesis.

Peroxisome biogenesis; Gene expression regulation; Ring finger; PAF-1

Shimozawa et al. [1] recently characterized the human peroxisome assembly factor-1 (PAF-1), an essential factor for the biogenesis of peroxisomes as shown in mutant cell lines and in a patient with Zellweger syndrome. PAF-1 is a peroxisome integral membrane protein and the deduced primary structures from both human and rat PAF-1 revealed two conserved putative membrane-spanning segments and seven cysteine residues in the carboxyl terminal region [1].

We would like to point out that the cysteine-rich carboxyl-terminal region of PAF-1 contains the conserved alignment of amino acid residues that characterizes a potential zinc and DNA-binding signature subsequence present in a family of proteins involved in site-specific recombination, DNA repair, and transcriptional regulation (Fig. 1) [2–4]. This conserved subsequence in PAF-1 may therefore be the key to a gene expression regulatory pathway important for peroxisome biogenesis since fibroblasts that do not express PAF-1 lack peroxisomes [1].

The carboxyl terminus of PAF-1 is predicted to face the luminal side of the peroxisome. One can hypothesize that PAF-1 could influence gene expression by also localizing to the nuclear membrane. Its carboxyl-terminus may then interact directly with DNA or dimerize with nuclear regulatory factors. Alternatively, the carboxyl-

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                 * **          * * **  *          ** *
                 C C           C   C C            C C
PAF-1            GKECALCGEWPTMPH-TIGCEHIFCYFCAKSSFLFDVYFTCPKCGTEV
HSV IE110        GDVCAVCTPEIAPHLDTFFPCMHRFCIPCMKTWMQL--RNTCPLCNAKL
T-LR             YGMCAVCREPWAEGAELLPCRHVFCTACVVQ------RWRCPSCQRRI
PE-38            KFECSVCLETYSQQSIPTTCDHGFCFKCVINLQSN--STVCPLCNTQV
RAD-18           LLRCHICKDFLKVPV-LTPCGHTFCSLCIRTHLNN--QPNCPLCLFEF
RPT-1            EVTCPICLELLKEPV-SADCNHSFCAACITLNYENG-KGNCPVCRVPY
SS-A/Ro          EVTCPICLDPFVEPV-SIECGHSFCQECISQVGKGG-GSVCAVCRQRF
RFP              ETTCPVCLQYFAEPM-MLDCGHNICCACLARCWGTT-NVSCPQCRETF
PML              FLRCQQCQAEAKCPK-LLPCLHTLCSGCLEAS-----GMQCPICQAPW
RAG-1            SISCQICEHILADPV-ETNCKHVFCRVCILRCLKVM-GSYCPSCRYPC
BMI-1            HLMCVLCGGYFIDATTITECLHSFCKTCIVRYLET--SKYCPICDVQV
RING-1           ELMCPICLDMLKNTMTTKECLHRFCSDCIVTALRSG-NKECPTCRKKL
VZV61            DNTCTICMSTVSDLGKTMPCLHDFCFVCIRAWTST--SVQCPLCRCPV
CG-30            KLQCNICFSVAEIKNELDTCKHQLCSMCIRKIRKRK-KVPCPLCRVES
CG30-rel         RLQCHICCSVGEIKNELHTCRHQLCVMCVRKIAQRK-RVECPMCRRKN
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Fig. 1. Alignment of carboxyl-terminus of human PAF-1 with the ring finger motif present in a family of proteins known or suspected to interact with DNA. Positions with conserved amino acids or conservative substitutions among all proteins are shown in bold letters and marked with asterisks. Positions of seven conserved cysteine residues are depicted with C. Similar amino acids or conservative substitutions with respect to the human PAF-1 sequence are underlined. Hyphens indicate gaps added for maximum alignment. References for sequences shown are cited in [2–4].

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terminus of PAF-1 may be cleaved off in the peroxisome and affect gene expression at the RNA level once it gains access to the cytoplasm of the cell. An intriguing possibility is that the carboxyl-terminus of PAF-1 could regulate expression of DNA from a parasitic or invading organism within the peroxisome. These hypotheses are testable with the available biological reagents.

## REFERENCES

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