# Stigmoid Body Articles

| | CITATION | ABSTRACT | NOTES |
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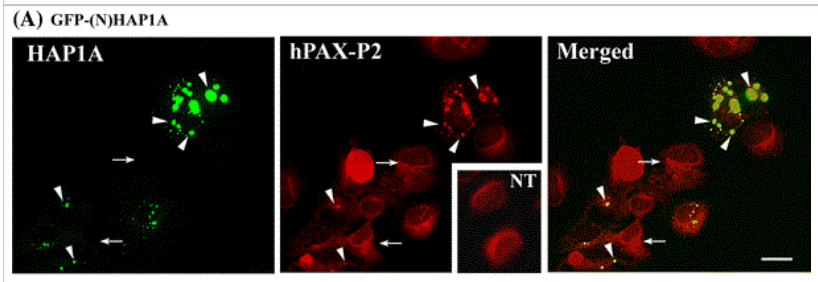
| blocked URL | Gutekunst, C., Li, S., Yi, H., Ferrante, R.J., Li, X., Hersch, S.M. (1998) The cellular and subcellular localization of huntingtin-associated protein 1 (HAP1): Comparison with huntingtin in rat and human. J Neuroscience 18(19):7674-86. | The cellular and subcellular distribution of HAP1 was examined in rat brain by light and electron microscopic immunocytochemistry and subcellular fractionation. HAP1 localization was also determined in human postmortem tissue from control and Huntington's disease (HD) cases by light microscopic immunocytochemistry. At the cellular level, the heterogeneity of HAP1 expression was similar to that of huntingtin; however, HAP1 immunoreactivity was more widespread. The subcellular distribution of HAP1 was examined using immunogold electron microscopy. Like huntingtin, HAP1 is a cytoplasmic protein that associates with microtubules and many types of membranous organelles, including mitochondria, endoplasmic reticulum, tubulovesicles, endosomal and lysosomal organelles, and synaptic vesicles. A quantitative comparison of the organelle associations of HAP1 and huntingtin showed them to be almost identical. Within HAP1-immunoreactive neurons in rat and human brain, populations of large and small immunoreactive puncta were visible by light microscopy. The large puncta, which were especially evident in the ventral forebrain, were intensely HAP1 immunoreactive. Electron microscopic analysis revealed them to be a type of nucleolus-like body, which has been named a stigmoid body, that may play a role in protein synthesis. The small puncta, less intensely labeled, were primarily mitochondria. These results indicate that the localization of HAP1 and huntingtin is more similar than previously appreciated and provide further evidence that HAP1 and huntingtin have localizations consistent with roles in intracellular transport. Our data also suggest, however, that HAP1 is not present in the abnormal intranuclear and neuritic aggregates containing the N-terminal fragment of mutant huntingtin that are found in HD brains. | |
|  | Fujinaga, R., Yanai, A., Nakatsuka, H., Yoshida, K., Takeshita, Y., Uozumi, K., Zhao, C., Hirata, K., Kokubu, K., Nagano, M., Shinoda, K., 2007. Anti-human placental antigen complex X-P2 (hPAX-P2) anti-serum recognizes C-terminus of huntingtin-associated protein 1A common to 1B as a determinant marker for the stigmoid body. Histochemistry and Cell Biology, 128: 335-48. | The anti-serum against an unknown human placental antigen complex X-P2 (hPAX-P2) immunohistochemically recognizes three putative molecules (*hPAX-P2S*, *hPAX-P2N*, and *hPAX-P2R*), each of which is associated with the stigmoid bodies (STBs), necklace olfactory glomeruli (NOGs), or reticulo-filamentous structures (RFs) in the rat brain. The STBs also contain huntingtin-associated protein 1 (HAP1), and the HAP1-cDNA transfection induces STB-like inclusions in cultured cells. In order to clarify the relationship between *hPAX-P2S* and HAP1 isoforms (A/B), we performed Western blotting, immuno-histo/cytochemistry for light- and electron-microscopy and pre-adsorption tests with HAP1 deletion fragments. The results showed that the anti-hPAX-P2 anti-serum recognizes HAP1$^{474\text{-}577}$ of HAP1A/B in Western blotting and strongly immunostains HAP1A-induced STB-like inclusions but far weakly detects HAP1B-induced diffuse structures in HAP1-transfected HEK 293 cells. In the rat brain, immunoreactivity of the anti-hPAX-P2 anti-serum for the STBs was eliminated by pre-adsorption with HAP1 $^{474\text{-}577}$, whereas no pre-adsorption with any different HAP1 fragments can suppress immunoreactivity for the NOGs and RFs, which were not immunoreactive to anti-HAP1 anti-serum. These findings indicate that *hPAX-P2S*, which is distinct from *hPAX-P2N* and *hPAX-P2R*, is identical with STB-constituted HAP1 and that the HAP1-induced/immunoreactive inclusions correspond to the hPAX-P2-immunoreactive STBs previously identified in the brain. | |
| blocked URL | Fujinaga, R., Takeshita, Y., Uozumi, K., Yanai, A., Yoshioka, K., Kokubu, K., Shinoda, K. (2009) Microtubule-dependent formation of the stigmoid body as a cytoplasmic inclusion distinct from pathological aggresomes. Histochem Cell Biol 132:305-318 | The stigmoid body (STB) is a neurocytoplasmic inclusion containing huntingtin-associated protein 1 (HAP1), an interactor of huntingtin, and its formation is induced by transfection of HAP1-cDNA into cultured cells. Although STB is believed to play a protective role in polyglutamine diseases, including Huntington's disease and spinal and bulbar muscular atrophy, by sequestering the causative proteins, huntingtin and androgen receptor, respectively, its physiological function and formation remain poorly understood. Therefore, STB is occasionally confused with another cytoplasmic inclusion observed in polyglutamine diseases, the aggresome. Here we examined the subcellular dynamics of STB and compared it immunohistochemically and cytochemically with the aggresome in the rat brain and COS-7 or HeLa cells transfected with HAP1 and/or polyglutamine disease-associated genes. In time-lapse image analysis of HAP1-transfected cells, the HAP1-induced STB is formed from multiple fusions of small HAP1 inclusions characterized by vigorous cytoplasmic movement. In HAP1-transfected cells treated with a microtubule-depolymerizing drug, although the formation of small HAP1 inclusions was not affected, their fusion was critically inhibited. Immunohistochemistry and cytochemistry revealed the absence of association between STB and aggresomal markers, such as ubiquitin/proteasome, intermediate filaments, and the centrosome. Taken together, we concluded that STB is formed by a two-step process comprising microtubule-independent formation of small HAP1 inclusions and microtubule-dependent fusion of these inclusions, and that STB is distinct from pathological aggresomes. | |

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