



University of
Salford
MANCHESTER

Cytosolic aminopeptidase P (APP-1): a possible role in meiotic progression in *Caenorhabditis elegans*.

Isaac, RE, Craig, H, Martinez-Perez, E and Brooks, DR

Title	Cytosolic aminopeptidase P (APP-1): a possible role in meiotic progression in <i>Caenorhabditis elegans</i> .
Authors	Isaac, RE, Craig, H, Martinez-Perez, E and Brooks, DR
Publication title	
Publisher	
Type	Conference or Workshop Item
USIR URL	This version is available at: http://usir.salford.ac.uk/id/eprint/9733/
Published Date	2009

USIR is a digital collection of the research output of the University of Salford. Where copyright permits, full text material held in the repository is made freely available online and can be read, downloaded and copied for non-commercial private study or research purposes. Please check the manuscript for any further copyright restrictions.

For more information, including our policy and submission procedure, please contact the Repository Team at: library-research@salford.ac.uk.

752B

Cytosolic Aminopeptidase P (APP-1): a possible role in meiotic progression in *Caenorhabditis elegans*. **Richard Elwyn Isaac**¹, Hannah Craig¹, Enrique Martinez-Perez², Darren Brooks³. 1) Faculty of Biological Sciences, Miall Building, University of Leeds, Leeds LS2 9JT, UK; 2) Department of Molecular Biology and Biotechnology, University of Sheffield, Firth Court, Western Bank, Sheffield S10 2TN, UK; 3) Biomedical Sciences Research Institute, School of Environment and Life Sciences, University of Salford, Salford M5 4WT.

Aminopeptidase P (APP) is a metallopeptidase that specifically removes amino acids from the N-terminus of peptides with a penultimate N-terminal proline residue. The cyclic structure of the proline side chain places a conformational restraint on peptide bonds in its vicinity, which therefore tend to be resistant to hydrolysis by non-specialist peptidases. APP is one of the few peptidases capable of cleaving peptide bonds involving a proline residue and therefore has an important role in protein/ peptide processing and catabolism. In humans, at least two APP genes exist, coding for a soluble cytosolic enzyme (APP-1) and a secreted membrane-bound form (APP-2). APP-2 has been the subject of much research due to its role in the regulation of blood pressure and potential as a drug target in the treatment of hypertension, but there is little information available on the biological role of APP-1. We have previously shown that a *C. elegans* APP-1::GFP fusion protein is strongly expressed as a cytosolic protein in the intestinal cells of late embryos, larvae and adult worms. Immunocytochemistry using antibodies specific for *C. elegans* APP-1 has confirmed the initial promoter-GFP expression pattern and has revealed additional strong expression of APP-1 in the female germline. We have obtained a *C. elegans* app-1 mutant (tm1715), generously provided by the Japanese National Bioresource Project, that has a 452 bp deletion spanning most of exon 2 and part of exon 3. We have shown that tm1715 is a null mutant by using a specific assay for APP aminopeptidase activity and by western blot analysis. Phenotypic analysis for tm1715 revealed a higher (18-fold) than normal number of males (XO) generated on self-fertilisation of the adult hermaphrodite (XX) and a 50 percent reduction in brood size. These phenotypes are similar to those seen in a sub-set of him mutants (high incidence of males) that are defective in segregation of autosomes as well as the X chromosome during meiosis. The APP-1 antibody gives diffuse staining inside meiotic nuclei of the female gonad and staining with anti-RAD-51 antibodies of app-1 mutants suggests an altered pattern in the repair of DNA double-strand breaks (DSBs) generated during meiotic prophase. These preliminary results suggest an important biological role for APP-1 in meiotic progression in *C. elegans*.