site, and CK2 inhibitors decrease endogenous levels of pS483/pS484-WASP. Cory *et al.* also showed that S483 and S484 are substrates for CK2 *in vitro*. S483/S484 phosphorylation enhanced VCA–Arp2/3 binding, and phosphorylation of S483/S484 enhanced actin polymerization that was induced by activated Cdc42 or by a Y291 mutation that renders WASP constitutively active. S483/S484 phosphorylation, therefore, seems to be important for optimal functioning of activated WASP.

So, as Cory *et al.* conclude, "…post-translational modification of WASP is important in its regulation … and it will be of great interest to determine the interplay between phosphorylation and other cellular regulators of WASP function".

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References and links

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PROTEOGLYCANS

A close-up of chondroitin

Chondroitin and heparan sulphate, two types of glycosaminoglycan, are well-known sugar polymers in animals. Much more is known about heparan sulphate's involvement during development compared with chondroitin sulphate's, but, thanks to two reports in *Nature*, chondroitin is at last in the spotlight, and is now shown to be involved in *Caenorhabditis elegans* cytokinesis and morphogenesis.

The so-called squashed vulva (*sqv*) genes are important for embryonic development and postembryonic vulval morphogenesis, and seven of these are known to regulate the biosynthesis of chondroitin and heparan sulphate. Hwang *et al.* cloned the eighth *sqv* gene, *sqv-5*, corresponding to the gene sequence *T24D1.1*, which Mizuguchi *et al.* also cloned in a separate study.

The protein encoded by *T24D1.1* is similar to both human chondroitin synthase and chondroitin *N*-acetylgalactosaminyltransferase, which are needed for the initiation and elongation of chondroitin chains, respectively. In *C. elegans*, though, SQV-5 — or chondroitin synthase (ChSy), as Mizuguchi *et al.* refer to it — carries out both functions; protein extracts prepared from worms homozygous for a *sqv-5* null allele lacked both activities. And both groups reported a marked reduction in the levels of chondroitin in the absence of *sqv-5*/*ChSy*.

Both groups used conventional mutations or RNA interference (RNAi) — by feeding the worms dsRNA — to suppress *sqv-5*/*ChSy* expression. RNAi caused weaker defects compared with conventional mutations; ~90% of embryos from RNAi-treated worms died whereas all embryos of conventional mutants died. Mizuguchi *et al.* also noticed that 60% of the survivors of RNAi treatment showed poor gonad formation and laid few, morphologically abnormal eggs. Hwang *et al.* reported that RNAi treatment reduced vulval extracellular spaces.

A closer look by Mizuguchi *et al.*, using four-dimensional microscopy, showed severe cell-division defects. Embryonic cell division seemed to progress and then reverse (from 2 to 4, to 6 cells, to 4, to 6 cells, and so on), apparently as a result of incomplete cytokinesis. Eggs laid after longer RNAi treatment, which had even less chondroitin, underwent normal nuclear division, but failed to undergo cytokinesis altogether. So, if chondroitin is required for normal embryonic cell division and cytokinesis, it follows, then, that treating normal embryonic cells with chondroitinase should also induce similar phenotypes — which was indeed the case.

Consistent with a role for chondroitin in cytokinesis, early embryogenesis and morphogenesis, Mizuguchi *et al.* showed that chondroitin was present in the oocytes, the uterus, spermatheca and fertilized egg shells. The cell surfaces of early embryos expressed high levels, too. Using anti-SQV-5 antibodies, Hwang *et al.* observed punctate staining in the cytoplasm of the vulva, uterus and oocytes, similar to the staining pattern that had previously been observed for SQV-1 and SQV-7. So Hwang *et al.* propose that the chondroitin biosynthetic steps that are catalysed by these SQV proteins all occur in the same subcellular compartment — most probably the Golgi apparatus.

Hwang *et al.* also propose that chondroitin's ability to interact with water, which would generate osmotic pressure, could well be responsible for its ability to expand extracellular space, on the basis that observed defects in the first embryonic cytokinesis and vulval morphogenesis occur concomitantly with a reduction in extracellular matrix size. Mizuguchi *et al.* also suggest that the role of chondroitin in cell division and cytokinesis could be a structural one, but raise the possibility that an unidentified chondroitin-dependent signalling event might be necessary for the completion of cytokinesis, and indicate that the possible relationship of chondroitin with components of the cell cycle and cytoskeleton requires investigation.

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References and links

ORIGINAL RESEARCH PAPERS Hwang, H.-Y. *et al. Caenorhabditis elegans* early embryogenesis and vulval morphogenesis require chondroitin biosynthesis. *Nature* **423**, 439–443 (2003) | Mizuguchi, S. *et al.* Chondroitin proteoglycans are involved in cell division of *Caenorhabditis elegans*. *Nature* **423**, 443–448 (2003)