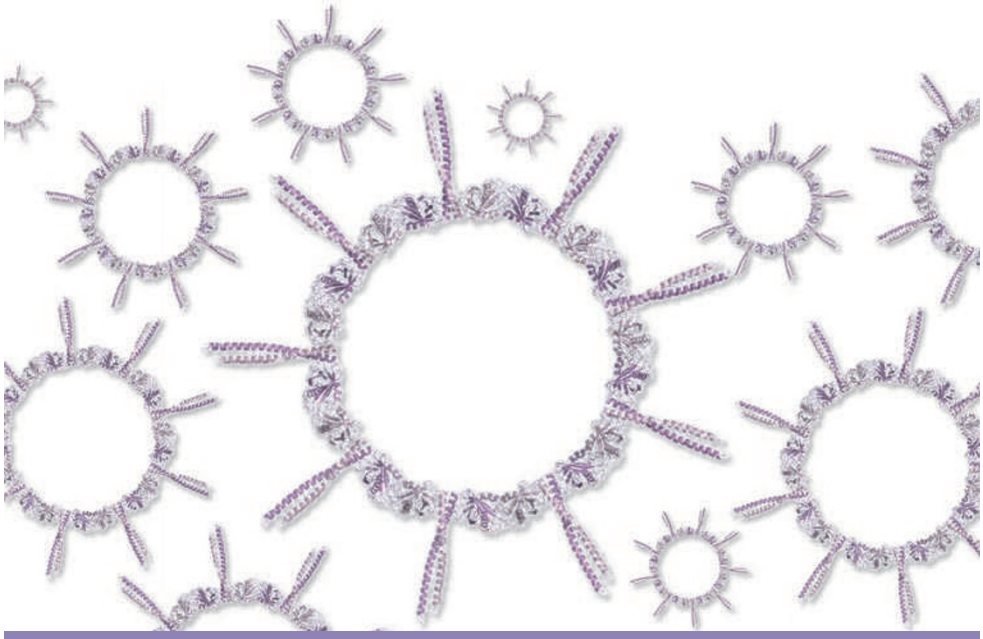

CYTOSKELETON

SAS-6 turns a cartwheel trick

Centrioles provide the core structure for generating centrosomes, cilia and flagella. They themselves undergo a complex biogenesis process, which begins with the formation of a 'cartwheel' structure, in which nine 'spokes' radiate from a central ring-like hub. Spindle assembly abnormal 6 (SAS-6), which is crucial for centriole assembly, localizes to the cartwheel in several species, and two groups now find that SAS-6 might drive cartwheel formation through assembly into oligomers.

Kitagawa *et al.* purified the evolutionarily conserved amino-terminal domain of SAS-6 from *Caenorhabditis elegans* and determined its crystal structure at 2.1 Å resolution. This revealed the presence of dimers of SAS-6, in which the conserved Ile154 residue localized to the interaction interface. van Breugel *et al.* determined the X-ray crystallography structure of an analogous N-terminal fragment of Sas6 from *Danio rerio* (N-Sas6$^{1–156}$) at 1.92 Å. Again, head-to-head dimers formed through conserved motifs, including Phe131, the equivalent residue to Ile154 in *C. elegans* SAS-6, and both groups went on to show that dimer formation is essential for SAS-6 function.

van Breugel *et al.* showed that mutation of key residues that localized to the dimer interface, including Phe131, disrupted dimerization. These sites were also important for efficient centrosomal localization of SAS-6 in human U2OS cells when transiently overexpressed and for normal flagellum formation in *Chlamydomonas reinhardtii*. Kitagawa *et al.* found that disruption of SAS-6 oligomerization by mutation of Ile154 or Phe131 prevented centriole formation in early worm embryos and human U2OS cells, respectively.

A structural model for the spindle assembly abnormal 6 (SAS-6) homologue BLD12 from *Chlamydomonas reinhardtii*. SAS-6 proteins form dimers through their coiled-coil domains, and subsequent association through their amino-terminal domains results in the formation of a ninefold symmetrical ring with a diameter similar to that of 'cartwheel' structures observed previously. Coiled-coil domains radiate out from the ring. Image is reproduced, with permission, from Kitagawa, D. *et al.* © (2011) Elsevier.

Both groups also solved the crystal structure of the N-terminal domain together with a part of the adjacent coiled coil. Combined with the structure of the N-terminal domain alone, this allowed a structural model to be built in which nine homodimers interact through adjacent N-terminal domains and assemble into a ring from which the coiled-coil domains radiate outwards.

Cryo-electron microscopy and rotary metal-shadowing electron microscopy allowed the two groups to ask how this oligomerization of SAS-6 relates to assembly of the early centriole structure. In both cases, the authors saw that the SAS-6 assemblies formed a ring-like structure with a diameter consistent with that observed *in vivo*, and radiating spokes that were consistent with the length of the predicted coiled coils. Together, these findings suggest that SAS-6 has an evolutionarily conserved role in establishing the ninefold symmetry of the centriole through its ability to oligomerize.

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ORIGINAL RESEARCH PAPERS Kitagawa, D. *et al.* Structural basis of the 9-fold symmetry of centrioles. *Cell* **144**, 364–375 (2011) | van Breugel, M. *et al.* Structures of SAS-6 suggests its organization in centrioles. *Science* 27 Jan 2011 (doi:10.1126/science.1199325)