

and if the transposase displaces polymer subunits that are nearby on the DNA, transposition will occur most frequently at distant sites. Daniel Voytas (Iowa State University, Ames, USA) reported that the Sir 3 and 4 genes, involved in silencing at the telomeres, direct yeast Ty5 to silent chromatin. And Nancy Craig (Howard Hughes Medical Institute/Johns Hopkins University, Baltimore, USA) reported that the TnsE pathway of Tn7 is biased to insert near double strand breaks and at replication termination sites. We imagine this is part of a strategy for Tn7 to get itself transferred onto a conjugating plasmid.

Several speakers discussed host suppression of transposition. Among them, Ronald Plasterk (Netherlands Cancer Institute, Amsterdam, The Netherlands) spoke on suppression of transposition in the germ-line of Bristol strains of *Caenorhabditis elegans*. Surprisingly, the suppression pathway overlaps with the RNAi pathway, a mysterious process by which exogenous double-stranded RNA blocks expression of the proteins it encodes. Silke Jensen (Institut Gustave Roussy, Villejuif, France) reported on suppression of I elements in *Drosophila*. Interestingly, transgenes containing fragments of I, whether in the sense or in the anti-sense direction, suppress invasion by a new I element. Joan Curcio (Wadsworth Center, Albany, USA) reported on inhibition of both Ty transposition and invasive growth by the yeast protein Fus3.

Zooming in from evolution to mechanism, several sessions focused on the assembly of protein–DNA complexes. Assembly is coupled to activation, to ensure that recombination occurs at the proper time and place and on the proper substrates. The crystal structure of Cre bound to a Lox Holliday junction, presented by Greg Van Duyne (University of Pennsylvania School of Medicine, Philadelphia, USA), explained how, of the four DNA molecules in a Holliday junction, only two at a time are activated to be cleaved. Phoebe Rice (University of Chicago, USA) presented the structure of FLP recombinase, confirming biochemical predictions that its catalytic tyrosine, unlike that of closely related Cre, is donated *in trans*; the tyrosine reaches into the active site of the neighboring subunit, to cleave the DNA bound by the neighbor. Similarly, William Reznikoff (University of Wisconsin, Madison, USA) reported that Tn5 transposase donates catalytic acidic residues (the DDE motif) *in trans*. This mechanism helps ensure that two distant DNA sites move together.

Transposons have evolved means to recognize themselves, to find a good insertion site, and to coordinate the cutting and pasting of their two ends: a complex series of tasks. And yet they must work with the tools they carry on their backs and the proteins they co-opt from their hosts. These elements are streamlined, and we see in them the beauty both of complexity and of simplicity.

Outlook LETTERS



Unified nomenclature for the COP9 signalosome and its subunits: an essential regulator of development

The COP9 signalosome was first identified in *Arabidopsis thaliana* as an essential regulator of light signal transduction¹. Subsequently, the COP9 signalosome was identified in animal systems, suggesting that this complex had a general role in developmental regulation^{2,3}. Genetic analysis in *Drosophila* indicated that this complex is essential for animal development⁴. This role might include the control of the cell cycle and regulation of MAP-kinase signaling^{3,5–10}. The biochemical purification of the COP9 signalosome from cauliflower¹¹, mammals^{9,16} and *Arabidopsis*¹² indicated that this complex comprises eight core subunits. The complex does not exist in *Saccharomyces cerevisiae* but appears to be present in *Schizosaccharomyces pombe*⁵. The COP9 signalosome is similar, both in size and composition, to two other regulatory complexes: the lid of the 19S proteasome regulatory particle and the eukaryotic translational regulatory complex eIF3 (Refs 13, 14). Most subunits from all three

complexes contain one of two structural motifs: the PCI/PINT domain and the MPN domain^{14,15}. Reports have suggested interactions between these complexes and/or their subunits³.

Because the genes encoding these subunits were isolated either through a variety of unrelated genetic screens, or by the biochemical purification of the complex from various organisms, the original names for the COP9 signalosome subunits are largely unrelated; in most cases, the names do not imply that the protein product is a COP9 signalosome subunit. The fact that many of the subunits have several names adds to the confusion. In order to clarify this situation, a unified subunit nomenclature was agreed upon that conveys the fact that these proteins function cooperatively within a specific complex, and that will be applicable for all organisms. The subunits from human, mouse and *Drosophila* have previously been numbered in decreasing size according to their

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apparent molecular weight, as measured by SDS-PAGE: Sgn1-8 (Ref. 9); COPS1-8 (Ref. 16); DCH1-8 (Ref. 4). The new designation keeps the same numbering system, while abbreviating COP9 signalosome to CSN. When needed, subunits from different organisms will be identified by the binomial prefix according to the species, such that subunit 1 from *Arabidopsis* would be AtCSN1. Gene families will be designated by the addition of a letter, and splicing variants by the addition of a second number after the letter. Accepted species-specific formats regarding the use of cases and italics for discrimination between genes, proteins and loci will be retained. The subunit composition of the COP9 signalosome and the proposed nomenclature are given in Table 1. A detailed listing is found in <http://www.tau.ac.il/botany/USR/chamovitz/csn.html>.

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TABLE 1. Summary of COP9 signalosome subunit previous and current nomenclature

New designation	Original nomenclature				
CSN1	<i>Arabidopsis</i> ^a COP11, FUS6	Human ^b Sgn1,GPS1	Mouse ^c COPS1, Mfh	<i>Drosophila</i> ^d DCH1	<i>S. pombe</i> ^e Caa1; Sgn ^{sp}
CSN2	Subunit 2	Sgn2, TRIP15, hAlien	COPS2	DCH2, Alien	Sgn ^{sp}
CSN3	Subunit 3	Sgn3	COPS3	DCH3	?
CSN4	COP8, FUS4	Sgn4	COPS4	DCH4	Sgn ^{sp}
CSN5	AJH1, AJH2	Sgn5, JAB1	COPS5, Jab1	DCH5	?
CSN6	Subunit 6	Sgn6, hYIP	COPS6	DCH6	?
CSN7	FUS5	Sgn7	COPS7a, COPS7b	DCH7	?
CSN8	COP9	Sgn8, hCOP9	COPS8	DCH8	?

^aRef. 3.

^bRefs 3, 9.

^cRef. 16.

^dRef. 4.

^e*Schizosaccharomyces pombe*; Ref. 5.

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Double trouble

In the assault on the genome, the favoured weapon these days is the single nucleotide polymorphism (SNP). Its very name implies that the underlying mode of sequence change is by one nucleotide at a time, and in studies of variation between species, which use sequence divergence as a molecular clock, the same assumption is often inherent.

Averof *et al.*¹ have examined coding sequences over long evolutionary time-scales to ask how frequently double-nucleotide substitutions occur. The amino acid serine is, uniquely, encoded

by two groups of codons (AGC/AGT and TCN) that cannot be interconverted by a single nucleotide substitution: interconversion must either be via one simultaneous double substitution, or two independent single events. The latter would introduce an intermediate altered amino acid – threonine (ACN) or cysteine (TGC/TGT). How frequent are interconversions at conserved serines, where intermediates are unlikely to have been well tolerated? In 23 homologous proteins in a wide range of eukaryotes and prokaryotes, they are widespread. Sequences outside coding

regions are expected to be less directly influenced by selection: on a relatively short time-scale within closely related primate species, double-nucleotide substitutions are found here too, at a significant excess over the expectation from adjacent single changes.

Together, these two surveys suggest that double-nucleotide changes occur more often than has been thought; molecular phylogeneticists and those who study human genetic disorders should take note.

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