The remarkable success reported by Grimes *et al.*[1] should stimulate structural biology at many levels. First, it provides a new paradigm for the assembly of complex virus particles. As mentioned, the concepts defined for BTVC assembly will almost certainly be found in the other members of the reoviridae family and similar principles may apply to other large and complex viruses. The novel feature of a sizing template and its surface properties should stimulate the exploration of antiviral agents that could disturb the required interactions for assembly. The technical success of solving a structure with such a large unit cell should inspire crystallographers to pursue larger complexes and to use crystals with exceptionally large unit cells when more conventional crystals do not come out of the crystallization trials. Finally, the work gives all of us the pleasure of enjoying the wonder of biology with its extraordinary use of chemical and physical principles to elegantly assemble such remarkable structures.

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1. Grimes, J.M. *et al. Nature,* **in the press** (1998).
2. Burroughs, J.N. *et al. J. Gen. Virol.* **75**,1849–1857 (1998).
3. Synchrotron Supplement, *Nature Struct. Biol.* **5**, 614– 654 (1998).
4. Grimes J.M. *et al. Structure* **5**, 885–893 (1997).
5. Grimes, J.M., Basak, A.K., Roy, P. & Stuart, D. X *Nature* **373**,167–170 (1997)..
6. Johnson, J.E. & Fisher AJ. *In Encyclopedia of Virology* (eds Webster, R. G. & Granoff. A.) 1573–1586 (Academic Press. London; 1994)
7. Caspar, D.L.D. & Klug, A. *Cold Spring Harbor Symp. Quant. Biol.* **27**, 1–24 (1962).
8. Johnson, J.E. & Speir, J. *J. Mol. Biol.* **269**, 665–675 (1997).
9. Burroughs, J.N. *et al. Virology* **210**, 217–220 (1995).
10. Speir, J.A. Munshi, S., Wang, G. Baker, T.S. & Johnson, J.E. 1995. *Structure* **3**,63–78.
11. Canady, M.A. *et al. Nature Struct. Biol.* **3**, 771–781 (1996).
12. McPherson, A. *J. Crystal Growth* **90**, 47–50 (1988).
13. Horne, R.W. *Adv. Virus Res.* **24**, 173–221 (1979).
14. Kapitakian, A.Z. & Chanock, R.M. In *Virology* (eds. B.N. Fields *et al.*) 1352–1404 (Raven, New York; 1990).
15. Estes, M.K. In *Virology* (eds. Fields, B.N. *et al.*) 1625–1655 (Lippincott-Raven, New York; 1996).
16. Shaw, A.L. *et al. Cell* **74**, 693–701 (1993).
17. Yeager, M. *et al. EMBO J.* **13**, 1011–1018 (1994).
18. Wickner, R. *J. Biol. Chem.* **206**,3797–3800 (1993).
19. Caston, J., Trus, B., Booy, F., Wall, J. & Steven, A. *J. Cell. Biol.* **138**, 975–985 (1997).
20. Liddington, R.C. *et al. Nature* **354**, 278–284 (1991).
21. Casjens, S. & Hendrix, R. *In* The Bacteriophages, (ed. Calendar, R.) 15–91 (Plenum Publishing Corp., New York; 1988).
22. Hendrix, R, & Duda R. *Adv. Virol. Res.* **50**, 235–288 (1998).
23. Duda, R. *Cell* **94**, 55–60 (1998).

picture story

Sex and the single male X chromosome

How is sex determined? In many species, the presence of two X chromosomes causes female development, and the presence of one, male development. A fundamental problem exists with such a system, however. How do the levels of essential transcripts from the X become equalized in males and females? In humans, dosage compensation occurs through transcriptional inactivation of one X chromosome per cell. But in Drosophila, the male X chromosome is hyper-transcribed approximately two-fold. Both systems involve altering chromatin structure, to make it either inaccessible or more accessible to the transcription machinery. A recent paper (Copps, K. *et al. EMBO J.*, **in the press**; 1998) analyzes a key event in formation of the Drosophila dosage compensation complex. These studies reveal an interaction that is interesting not only for its role in chromatin regulation but also for its potential to add to general knowledge about protein–protein interaction motifs.

In Drosophila males, a multiprotein complex, which may also contain the non-coding RNAs roX1 and roX2, mediates hyper-transcription of the X. Several protein components of this complex were identified from genetic screens for mutations with recessive, male specific lethal (MSL) phenotypes. Intriguingly, immunostaining of polytene chromosomes from the salivary glands of a male shows that the MSL complex (visualized using a fluorescently tagged antibody against MSL1; in green) and mono-acetylated histone H4 (in red) co-localize (yellow) and are found only on the X chromosome at hundreds of specific sites. Since histone acetylation is often associated with increased transcription, a major function of the MSL protein complex may be to target a histone acetyltransferase to the X chromosome. In support of this, the MOF protein, also identified from a male lethal screen (MOF stands for males absent on the first) is a probable acetyltransferase that may interact with the MSL complex.

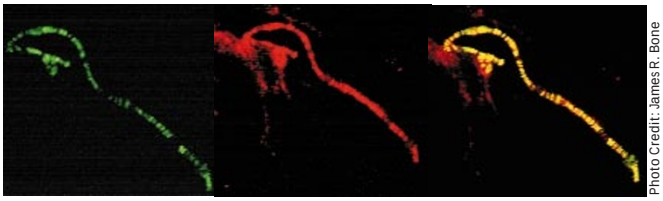

Photo Credit: James R. Bone

The MSLs can be co-immunoprecipitated, and work on purifying the complex for biochemical characterization is just beginning. Interactions between two MSL proteins, MSL1 (a novel acidic protein) and MSL2 (a putative zinc binding protein), are thought to be particularly important for initiating complex formation. Neither MSL1 nor MSL2 binds independently to the X chromosome and if either is non-functional, the other MSLs do not bind to any sites. Furthermore, ectopic expression of male specific MSL2 in females causes MSL complexes to form on the X chromosomes.

Copps *et al.* present yeast two-hybrid results which show that a fragment of MSL2, which contains a zinc binding RING finger domain, mediates a direct interaction with MSL1. Mutations that disrupt the MSL1–MSL2 interaction, identified from 'reverse two-hybrid assays' that select against productive protein–protein contacts, cluster around the MSL2 RING finger domain. Additionally, two *msl2* mutant alleles isolated from genetic screens are located near the first zinc binding site of the RING finger and these mutations, when tested in the yeast two-hybrid assays, disrupt the MSL1–MSL2 interaction.

RING finger domains are found in many proteins and have been postulated to be involved in DNA binding, RNA binding and protein–protein interactions, suggesting that the RING finger structure may provide a flexible template suitable for many purposes. Although the structures of isolated RING finger domains are known, no RING finger–target structure has been determined. Therefore, the MSL1–MSL2 interaction provides an opportunity for studying RING finger protein–protein interactions that are likely to be relevant *in vivo* — and supplies a starting point for understanding, in molecular detail, key events that mediate global and stable regulation of chromatin structure. **TS**