gation, perhaps through defects in chromosome condensation (*19*). The *Schizosaccharomyces pombe swi6* gene maintains transcriptional repression at centromeres and silent mating-type loci. Mutations in *swi6* not only interfere with silencing, but also cause a high rate of chromosome loss during mitosis (*20*, *21*) correlated with lagging centromere migration during anaphase (*22*). The colocalization of Swi6p with heterochromatin-like domains of centromeres, telomeres, and the silent mating-type loci suggests a structural role for Swi6p in gene expression and chromosome segregation (*20*). The composition of a *C. elegans* dosage compensation complex (*7*) suggests that it modifies the structure of X chromosomes to reduce gene expression. DPY-26 may similarly exert its effects on meiotic chromosome segregation through changes in chromosome structure.

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11. The *dpy-26* gene had been mapped to linkage group IV, between *unc-22* and *unc-31* (*9*). To map *dpy-26* more precisely, we used cosmids W03F2 and C03F9, which are flanked by *unc-22* and *unc-31*, as probes to identify polymorphisms between Bristol N2 and Bergerac N62 strains. We mapped *dpy-26* relative to these two polymorphisms by analyzing the DNA from Unc non-Dpy recombinants picked from the strains *dpy-26(n199) unc-31*/++N62 and *unc-22 dpy-26(n199)*/++N62. Of the *unc-31* recombinants, 20 had the N62 version of C03F9, and 5 had the N2 version. Of the *unc-22* recombinants, 26 had the N62 version of W03F2, and 4 had the N2 version. Thus, *dpy-26* mapped 0.18 map units (mu) to the left of C03F9 and 0.05 mu to the right of W03F2. Overlapping cosmids that form a contiguous link between C03F9 and W03F2 (100 μg/ml) were injected into gonads of *dpy-26(n199) unc-31(e169)/unc-22* heterozygotes with the dominant injection marker *rol-6* (100 μg/ml) [C. C. Mello, J. M. Kramer, D. Stinchcomb, V. Ambros, *EMBO J.* **10**, 3959 (1991)]. Lines that stably transmitted the dominant *rol-6* marker were isolated, and *dpy-26 unc-31* mutant offspring were tested for rescue of lethality. Overlapping cosmids C25G4 (7 of 7 lines) and C01G3 (6 of 6 lines) rescued the XX-specific lethality. The *dpy-26* rescuing region was narrowed to an 8.5-kb Sal I fragment of C25G4, pS2 (6 of 6 lines).
12. A 3.5-kb cDNA clone (pJL2) was obtained from a mixed-stage cDNA library screened with the 8.5-kb pS2 fragment. To obtain the 5′ end of the cDNA, we amplified the 5′ 375 base pairs (bp) by reverse transcriptase polymerase chain reactions (RT-PCR) using primers specific for the SL1 (5′-TCTAGAATTCCGCGGTTTAATTACCCAAGTTTG-3′) or SL2 (5′-TCTAGAATTCCGCGGTTTTAACCCAGTTACTC-3′) trans-splice leaders and a primer specific for *dpy-26*, JDL8 (5′-CCACTCGAGAGAGCTGAATCAAT-3′). The *dpy-26* transcript is trans-spliced to both SL1 and SL2 RNA leaders, suggesting that *dpy-26* may be a member of an operon [T. Blumenthal, *Trends Genet.* **11**, 132 (1995)]. The *dpy-26* genomic and cDNA clones were sequenced [M. Strathmann *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **88**, 1247 (1991)] and the *dpy-26* cDNA sequence in GenBank (accession number U43562) and genomic sequence (accession number Z70680) were deposited.
13. Cloned *Pfu* polymerase was used with primers JDL18 (5′-TTCTCCTGCTTTCTATTATCTAA-3′) and JDL19 (5′-CTTACTCATCCATCTGCTCAT-3′) in a PCR to amplify the first 2200 bp of *dpy-26* from single *dpy-26(n199)* homozygous mutant worms. PCR products from two independent reactions were cloned and sequenced on both strands.
14. Fragments of pJDL2 corresponding to amino acids 127 to 739 and 739 to 1263 of DPY-26 were subcloned into the T7 expression vector pRSET A (Invitrogen) fused to an epitope encoding six histidines. Expression of histidine-tagged DPY-26 fragments was induced in *Escherichia coli* BL21 pLys-S cells with 1 mM isopropyl-β-D-thiogalactoside, and the protein was purified by nickel-chelate chromatography and polyacrylamide gel electrophoresis. Mice received subcutaneous injections of 10 μg of protein mixed with Ribi adjuvant (RIBI ImmunoChem Research); rabbits received injections of 100 to 500 μg of protein mixed with Freund's adjuvant. All staining was performed with affinity-purified antibody. No staining was observed in wild-type embryos treated with preimmune sera.
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Sex-Specific Assembly of a Dosage Compensation Complex on the Nematode X Chromosome

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In nematodes, flies, and mammals, dosage compensation equalizes X-chromosome gene expression between the sexes through chromosome-wide regulatory mechanisms that function in one sex to adjust the levels of X-linked transcripts. Here, a dosage compensation complex was identified in the nematode *Caenorhabditis elegans* that reduces transcript levels from the two X chromosomes in hermaphrodites. This complex contains at least four proteins, including products of the dosage compensation genes *dpy-26* and *dpy-27*. Specific localization of the complex to the hermaphrodite X chromosomes is conferred by XX-specific regulatory genes that coordinately control both sex determination and dosage compensation.

Dosage compensation is an essential chromosome-wide regulatory process that modulates the expression of numerous genes related solely by their linkage to the same chromosome. The need for dosage compensation arises in organisms whose sex-determination mechanisms cause males (typically XO or XY) and females (typically XX) to differ in their dose of X chromosomes. Dosage compensation equalizes expression of most X-linked genes between the sexes despite the twofold difference in X-chromosome dose, thereby preventing the sex-specific lethality that would otherwise result from inappropriate amounts of X-chromosome products. This global modulation of gene activity is superimposed upon gene-specific regulation that allows X-linked genes to be expressed in specific tissues, at particular times, and in the correct sex (*1*).

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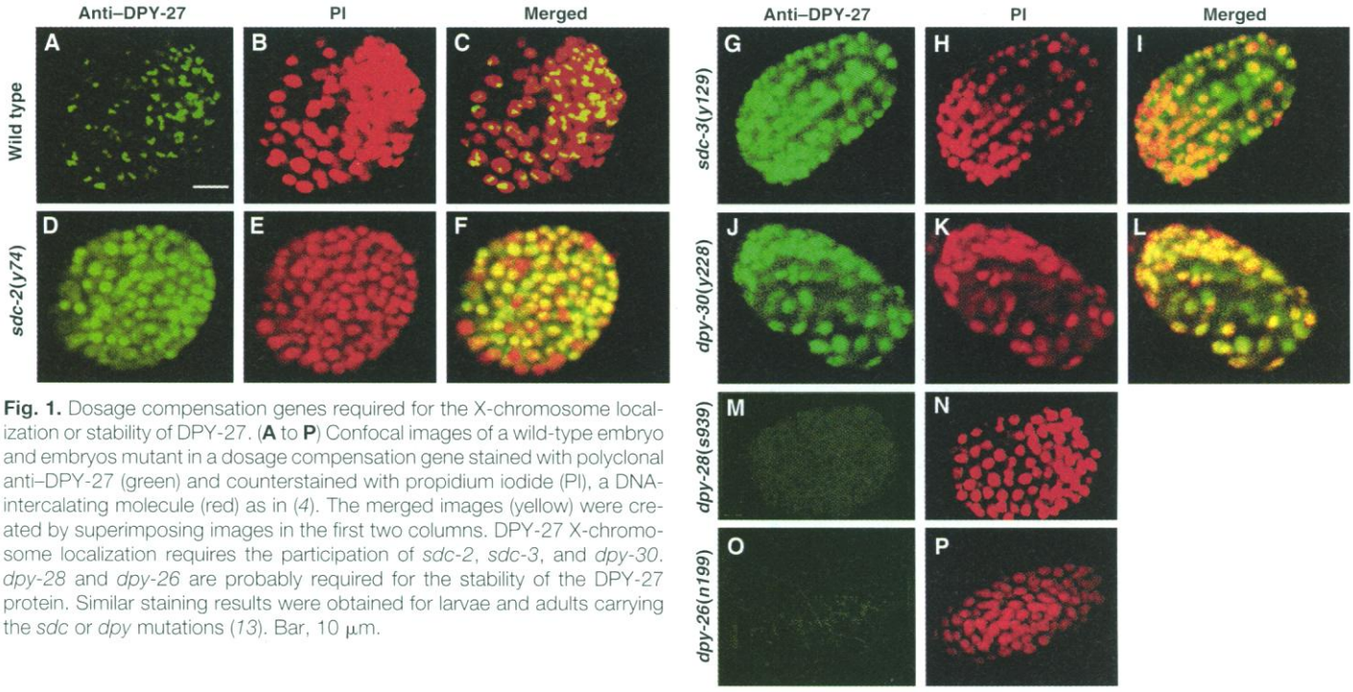

Fig. 1. Dosage compensation genes required for the X-chromosome localization or stability of DPY-27. (**A** to **P**) Confocal images of a wild-type embryo and embryos mutant in a dosage compensation gene stained with polyclonal anti–DPY-27 (green) and counterstained with propidium iodide (PI), a DNA-intercalating molecule (red) as in (*4*). The merged images (yellow) were created by superimposing images in the first two columns. DPY-27 X-chromosome localization requires the participation of *sdc-2*, *sdc-3*, and *dpy-30*. *dpy-28* and *dpy-26* are probably required for the stability of the DPY-27 protein. Similar staining results were obtained for larvae and adults carrying the *sdc* or *dpy* mutations (*13*). Bar, 10 μm.

In the nematode C. *elegans*, dosage compensation is achieved by halving the level of transcripts from each of the two hermaphrodite X chromosomes (*2*–*4*). Central to this process is the sex-specific localization of the DPY-27 dosage compensation protein to both hermaphrodite X chromosomes after the 30-cell stage of embryogenesis (*4*) (Fig. 1, A to C). DPY-27 is also produced and localized to the nuclei of males, but in this sex does not bind to the X chromosome (*4*). DPY-27 is a member of the evolutionarily conserved SMC (structural maintenance of chromosomes) family of proteins that participate in several aspects of chromosome dynamics, including chromosome condensation in yeast and frogs, as well as chromosome segregation in yeast (*4*, *5*). SMC proteins are characterized by an NH_2-terminal adenosine triphosphate (ATP)–binding motif, a conserved COOH-terminal domain, and a central coiled-coil region reminiscent of motor proteins such as myosin and kinesin. The similarity of DPY-27 to the SMC proteins, together with its X localization, suggests that DPY-27 promotes the reduction in X-chromosome transcript levels by inducing partial X-chromosome condensation during interphase of the cell cycle. To understand the mechanism of C. *elegans* dosage compensation, we examined how DPY-27 becomes localized to the X chromosome in a sex-specific manner and identified proteins that interact with DPY-27 on X to reduce X-chromosome expression.

We first investigated whether mutations in the gene hierarchy that controls dosage compensation interfered with the X localization or function of DPY-27. This hierarchy includes XX-specific genes that coordinately control both sex determination and dosage compensation (*sdc-1*, *sdc-2*, and *sdc-3*) (*6*–*8*) and genes that regulate only dosage compensation (*dpy-21*, *dpy-26*, *dpy-27*, *dpy-28*, and *dpy-30*) (*2*, *3*, *9*). Hermaphrodite-specific lethality results from the failure to activate these genes and the consequent increase in X-chromosome gene expression. Male-specific lethality results from the failure to inactivate the *sdc* and *dpy* genes and the consequent reduction in X-chromosome gene expression. In males, the activities of the *sdc* and *dpy* genes are repressed by *xol-1* (XO lethal) (*10*), a gene target (*11*) of the primary sex-determination signal, the ratio of X chromosomes to sets of autosomes (X:A).

Because mutations in most *sdc* and *dpy* genes cause >95% lethality in XX animals, we examined the staining pattern produced by antibodies to DPY-27 (anti–DPY-27) in XO mutants that lack *xol-1* and thereby activate the hermaphrodite mode of dosage compensation. Death of these *xol-1* XO mutants is prevented by a mutation in an *sdc* or *dpy* gene that blocks the execution of dosage compensation (*12*). Because mutations in *xol-1* permit DPY-27 to localize inappropriately to the male X chromosome (*4*), comparison of the anti–DPY-27 staining pattern between the *sdc* or *dpy xol-1* XO mutants and wild-type XX hermaphrodites reflects the impact of the dosage compensation mutation on DPY-27 in XX animals.

Analysis by confocal microscopy revealed that in embryos lacking *sdc-2*, *sdc-3*, or *dpy-30* activity, DPY-27 was distributed diffusely throughout interphase nuclei (Fig. 1, D to L) in a pattern indistinguishable from that seen in wild-type XO animals and in young XX embryos that have not yet activated dosage compensation. Thus, *sdc-2*, *sdc-3*, and *dpy-30* are all essential for the localization of DPY-27 to X. These results also indicate that the coordinate control genes activate the early steps of dosage compensation by recruiting DPY-27 to the X chromosome.

In contrast to *sdc-2*, *sdc-3*, and *dpy-30*, the dosage compensation genes *dpy-26* and *dpy-28* affect the production or stability of DPY-27, whereas the coordinate control gene *sdc-1* and the dosage compensation gene *dpy-21* affect other aspects of dosage compensation. Null mutations in *sdc-1* and *dpy-21* have no effect on the DPY-27 staining pattern (*13*), consistent with the minor dosage compensation disruption caused by these mutations. Null mutations in either *dpy-26* or *dpy-28* abolished anti–DPY-27 staining (Fig. 1, M to P), consistent with the XX-specific lethality caused by these mutations. To exclude the possibility that the lack of staining in *dpy-26* and *dpy-28* mutant embryos is due to a general reduction in protein synthesis, we also stained these embryos with antibodies specific for two other nuclear proteins (UNC-86 and EGL-43) and obtained a pattern indistinguishable from that of wild-type embryos (*13*).

To determine whether the absence of DPY-27 protein in *dpy-26* or *dpy-28* mutants reflected reduced levels of *dpy-27*

transcripts, we analyzed polyadenylated RNA from mutant embryos on Northern blots (*14*) using a *dpy-27* cDNA probe (Fig. 2). The slight reduction in *dpy-27* transcript levels in the *dpy-26* and *dpy-28* mutants cannot account for the absence of DPY-27 protein. Thus, loss of *dpy-26* and *dpy-28* reduces either the translation or the stability of DPY-27. If DPY-26 and DPY-28 function by forming a complex with DPY-27, then DPY-27 might become unstable in the absence of these protein partners. Precedence for such destabilization exists in the *Drosophila* dosage compensation pathway, which also involves the formation of a protein complex that is localized to X in a sex-specific manner (*15*). According to this hypothesis, the C. *elegans* dosage compensation complex would have to form and stabilize DPY-27 in both sexes independently of its association with X to account for the abundance of DPY-27 in XO embryos.

We tested the hypothesis that DPY-27 forms a stable complex with DPY-26 by immunoprecipitation experiments with affinity-purified anti–DPY-27 or anti–DPY-26 (*4*, *16*) using nuclear extracts (*17*) from wild-type and mutant embryos. The resultant immunoprecipitates were fractionated by SDS–polyacrylamide gel electrophoresis (PAGE) and immunoblotted with anti–DPY-27 or anti–DPY-26. As expected, anti–DPY-27 immunoprecipitated DPY-27 from wild-type nuclear extracts but not from *dpy-27* mutant extracts (Fig. 3A, lanes 1 and 2). Anti–DPY-27 also immunoprecipitated DPY-26 from wild-type extracts but not from *dpy-27* mutant extracts (Fig. 3A, lanes 5 and 6), demonstrating that DPY-27 and DPY-26 form a stable complex that withstands 400 mM KCl. Conversely, anti–DPY-26 immunoprecipitated both DPY-26 and DPY-27 from nuclear extracts of wild-type embryos (Fig. 3A, lanes 7 and 8), confirming the existence of the DPY-27–DPY-26 complex. Anti–DPY-27 did not immunoprecipitate DPY-27 from nuclear extracts deficient in DPY-26 or DPY-28 (Fig. 3A, lanes 3 and 4), as expected based on the immunofluorescence experiments. Similarly, DPY-26 and DPY-27 were not detected in immunoblots of nuclear extracts deficient in DPY-26, DPY-27, or DPY-28 (*13*). These experiments provide evidence that DPY-26 and DPY-27 form a complex and suggest that DPY-28 is also part of that complex.

To identify other components of the dosage compensation complex, we partially purified the complex from wild-type and *dpy-27* mutant nuclear extracts with ion-exchange chromatography (*18*). The fractions that contained DPY-27 were then immunoprecipitated with either anti–DPY-26 or anti–DPY-27 and the proteins separated by SDS-PAGE (Fig. 3B). Comparison of the proteins immunoprecipitated from the wild-type and the *dpy-27* mutant extracts revealed at least four proteins specific to the dosage compensation complex. Two proteins migrating at ~170 kD were identified as DPY-26 and DPY-27 by immunoblot analysis (Fig. 3C). Two other proteins migrated at ~160 kD and ~150 kD. One may be DPY-28, because mutations in the *dpy-28* gene affect the stability of the complex, but the identity of the other protein is unknown.

To assess the native size of the protein complex, we fractionated crude wild-type nuclear extract by centrifugation through a 15 to 60% sucrose gradient and then immunoblotted the fractions with anti–DPY-26 and anti–DPY-27. DPY-26 and DPY-27 comigrated in the gradient with a mobility between that of the 443- and 669-kD molecular size standards, consistent with the estimated size of the partially purified complex.

The results of our biochemical and immunofluorescence experiments, together with the DPY-26 experiments in the accompanying report (*16*), demonstrate that C. *elegans* achieves dosage compensation through a protein complex that specifically localizes to the X chromosomes of hermaphrodites to reduce their gene expression. Our studies also identify proteins pivotal to the sex-specific localization of DPY-27 and presumably other complex members to the X chromosome. These results suggest the following model: In males, the dosage compensation complex is prevented from associating with X by the male-specific *xol-1* gene, which represses *sdc* gene activity. In hermaphrodites, *sdc-2*, in conjunction with *sdc-3* and *dpy-30*, activates dosage compensation by localizing the protein complex to X. *sdc-2* is the candidate gene to trigger the dosage compensation process and to confer hermaphrodite specificity, because its product is present exclusively in XX animals, unlike the others (*8*, *19*). SDC-3 might itself associate with X to direct DPY-27 localization, because it contains a pair of TFIIIA-type zinc finger motifs that are essential for dosage compensation (*7*, *14*). Finally, the small, nuclear DPY-30 protein probably influences the localization of DPY-27 to X indirectly (*20*), by affecting the activity of *sdc-3* (*21*). Through these studies, a picture has emerged of how the genes of the dosage compensation hierarchy act at the molecular level to equalize X-chromosome expression between the sexes.

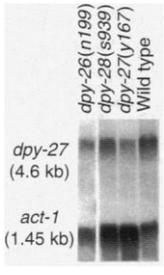

Fig. 2. *dpy-27* transcript levels in dosage compensation mutants. Polyadenylated RNA was isolated from wild-type, *dpy-26* (*n199*), *dpy-28*(*s939*), and *dpy-27*(*y167*) embryos as in (*14*). The filter-bound mRNAs were hybridized with a probe made from full-length *dpy-27* cDNA and an actin probe specific for *act-1* as a loading control. The reduced *dpy-27* transcript level in the *dpy-27*(*y167*) nonsense mutant probably reflects the instability of the mRNA in the absence of translation.

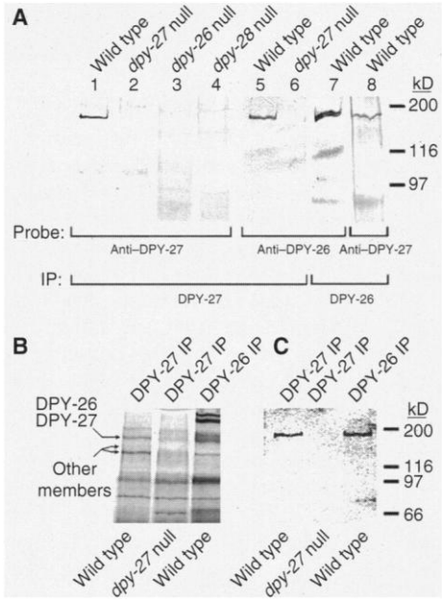

Fig. 3. A dosage compensation protein complex. (**A**) Coimmunoprecipitation of DPY-26 and DPY-27. Immunoprecipitations (IP) with wild-type and mutant nuclear extracts and anti–DPY-26 or anti–DPY-27 (*17*). The immunoprecipitates were analyzed by SDS-PAGE and immunoblotted with anti–DPY-26 or anti–DPY-27. Two isoforms of DPY-26 are observed. Anti–DPY-27 staining is not detectable in embryos with the *dpy-27* nonsense mutation used in these experiments (*4*). (**B**) Identification of additional dosage compensation complex members. After partial purification (*19*), the protein complex was analyzed by SDS-PAGE and silver-stained. Arrows indicate the locations of DPY-26, DPY-27 (both ~170 kD), and two other proteins (~160 and ~150 kD) whose copurification was dependent on DPY-27. (**C**) Immunoblot with an anti–DPY-26 probe shows that the DPY-26–DPY-27 complex is intact after the partial purification. Molecular size standards are indicated on the right (in kilodaltons).

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12. The *sdc-2* (*y74* or *y82*) and *sdc-3(y126)* null alleles cause such extensive XX-specific lethality and masculinization that mutants must be grown as *her-1(hv1y101); xol-1(y9) sdc* XO hermaphrodite strains. The XO-specific lethality caused by an *xol-1* mutation is suppressed by an *sdc* mutation, and the rescued XO animals are transformed into fertile hermaphrodites by a *her-1* mutation. The viable XO embryos and dying XX embryos were analyzed from this strain. Strains of *dpy-28(s939)* and *dpy-26(y65* or *n199)* null mutants did not require *her-1* because *dpy; xol-1* XO animals are hermaphrodites. We confirmed the results from the XO strains by examining anti–DPY-27 staining in a small sample of XX embryos from XX mutant mothers. The temperature-sensitive *dpy-30(y228)* and *dpy-28(y1)* XX mutants were grown as in (*20*). Because 30% of *sdc-3(y129)* XX mutants and all of the *sdc-1(n485)* and *dpy-21(e428)* mutants are viable, they were grown as XX strains.
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17. Nuclei were prepared at 4°C; all buffers were supplemented with 1 mM dithiothreitol, 0.1% aprotinin, 0.2 mM phenylmethylsulfonyl fluoride (PMSF), 1 mM benzamidine, 1 mM sodium metabisulfite. Embryos (*14*) were resuspended in 3 ml of homogenization buffer [15 mM K Hepes (pH 7.6), 10 mM KCl, 5 mM $MgCl_2$, 0.1 mM EDTA, 350 mM sucrose] per wet gram and homogenized with 0.5-mm glass beads in a beadbeater (Biospec) for 7 min. The homogenate was filtered through 20-μm-diameter nylon mesh and centrifuged for 5 min at 900 rpm (SS-34 rotor). The supernatant was adjusted to 0.2% NP-40 and centrifuged for 15 min at 8000 rpm (SS-34 rotor). The pellet was resuspended in 5 ml of homogenization buffer per gram of starting embryos, transferred to a cold glass dounce (Kontes), dispersed with a type B pestle, and centrifuged for 15 min at 8000 rpm (SS-34 rotor). The pellet was resuspended in 30 ml of buffer A [15 mM K Hepes (pH 7.6), 60 mM KCl, 5 mM $MgCl_2$, 0.1 mM EDTA, 0.5 mM EGTA, 1.5 M sucrose] and dispersed as before. Nuclei were layered onto 7 ml of buffer A with 2.1 M sucrose and centrifuged for 2 hours at 24,500 rpm in an SW28 (Beckman) rotor. The pellet was washed and resuspended in homogenization buffer. For immunoprecipitations, 50 μg of affinity-purified anti–DPY-27 (specific for the first 409 amino acids) or anti–DPY-26 (specific for amino acids 739 to 1263) were added to 80 μl of protein A–Sepharose (Pharmacia) equilibrated in HEMK buffer [25 mM K Hepes (pH 7.6), 200 mM KCl, 12.5 mM $MgCl_2$, 0.1 mM EDTA, 10% glycerol, 0.2 mM PMSF, and 0.1% NP-40] and incubated for 3 hours at 4°C with rocking. Embryonic nuclei (100 to 300 mg) in HEMK buffer were sonicated and microcentrifuged at 14,000 rpm for 30 min at 4°C. The supernatant was preincubated with protein A–beads, centrifuged as above, and added to the antibody–protein A complexes. After 4 hours at 4°C with rocking, the antibody–protein A complexes were washed twice (15 min each) in HEMK buffer and twice in HEMK buffer with 400 mM KCl. The bound proteins were analyzed by SDS-PAGE.
18. Partial purification of a dosage compensation complex: Nuclei (1 g) were resuspended in HEMK buffer, sonicated, and microcentrifuged at 14,000 rpm for 30 min at 4°C. The supernatant was added to SP-Sepharose resin (1 ml) and incubated for 1 hour at 4°C with rocking. The protein complex was washed with HEMK buffer and eluted from a column with HEMK buffer containing 400 mM KCl. The eluate was adjusted to 200 mM KCl, added to Q-Sepharose resin, and the mixture treated as above. The fractions containing DPY-27 were immunoprecipitated with anti–DPY-26 or anti–DPY-27 as described (*17*). Resins (Pharmacia) were washed with HEMK buffer containing 400 mM KCl and then HEMK buffer before use.
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21. *dpy-30* probably exerts its effects on dosage compensation through regulation of *sdc-3*. *sdc-3* XX null mutants do not exhibit a sex-determination defect, even though *sdc-3* functions in sex determination (*7*). The sex determination defect is apparent in *sdc-3*(null); *xol-1* XO animals, which are males. In contrast, *xol-1* XO animals are hermaphrodites if also mutant in *dpy-26*, *dpy-27*, or *dpy-28*. *dpy-30* mutations behave like *sdc-3* null mutations in that extensive masculinization is apparent only in the *dpy-30; xol-1* XO animals (*3*). For comparison, *sdc-2* XX mutants are very masculinized.
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Molecular Mimicry of Human Cytokine and Cytokine Response Pathway Genes by KSHV

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Four virus proteins similar to two human macrophage inflammatory protein (MIP) chemokines, interleukin-6 (IL-6), and interferon regulatory factor (IRF) are encoded by the Kaposi's sarcoma–associated herpesvirus (KSHV) genome. vIL-6 was functional in B9 proliferation assays and primarily expressed in KSHV-infected hematopoietic cells rather than KS lesions. HIV-1 transmission studies showed that vMIP-I is similar to human MIP chemokines in its ability to inhibit replication of HIV-1 strains dependent on the CCR5 co-receptor. These viral genes may form part of the response to host defenses contributing to virus-induced neoplasia and may have relevance to KSHV and HIV-I interactions.

Kaposi's sarcoma–associated herpesvirus (KSHV) is a gammaherpesvirus (*1*, *2*) related to Epstein-Barr virus (EBV) and herpesvirus saimiri (HVS). It is present in nearly all KS lesions including the various types of HIV-related and HIV-unrelated KS (*1*, *3*, *4*). Moreover, viral DNA is localized to KS tumors (*1*, *4*, *5*) and serologic studies show that KSHV is specifically associated with KS (*2*, *6*–*8*). Taken together, these studies indicate that KSHV is the probable infectious agent precipitating KS in patients with and without HIV (*9*). Related lymphoproliferative disorders, which can occur in patients with KS [such as body-cavity-based/primary effusion lymphoma (PEL), a rare B cell lymphoma, and some forms of Castleman's disease] are also associated with KSHV infection (*10*).

To identify viral genes in the KSHV genome, genomic sequencing (*11*) was performed with Supercos-1 and Lambda FIX II genomic libraries from BC-1, a non-Hodgkin's lymphoma cell line stably infected with both KSHV and EBV (*12*). The KSHV DNA fragments KS330Bam and KS631Bam (*1*) were used as hybridization starting points for mapping and bi-directional sequencing (*11*). Open reading frame (ORF) analysis (*13*) of the Z6 cosmid sequence identified two separate potential coding regions (ORFs K4 and K6) with sequence similarity to β-chemokines and a third potential coding region (ORF K2) similar to human interleukin-6 (huIL-6); a fourth potential coding region (ORF K9) is present in the Z8 cosmid insert sequence with sequence similarity to interferon regulatory factor (IRF) proteins (Fig. 1). None of these KSHV genes are similar to other known viral genes (*14*) and the predicted proteins were named without reference to their potential in vivo functional properties.

The 289-bp ORF of the K6 gene encodes a 10.5-kD predicted protein (vMIP-I) with 37.9% amino acid identity (71% similarity) to huMIP-1α and slightly greater differences with other β-chemokines (Fig. 1A). ORF K4 also encodes a predicted 10.5-kD protein (vMIP-II), similar in sequence and amino acid hydrophobicity

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