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Abstract Book

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diseases and how they potentially alter interactions with partner proteins. An *in silico* analysis of disease-related amino acid substitutions in lamins A/C revealed no apparent correlation between the location of the amino acid substitution and disease phenotype. Molecular modeling revealed that specific amino acid residues altered in disease mapped to potential protein partner interaction sites.
To test the predictions of our *in silico* analysis of protein partner interactions, we focused on amino acid residue R249 in the rod domain, which when altered to a Q causes Emery-Dreifuss muscular dystrophy. The equivalent amino acid substitution (R264Q) was modeled into the Drosophila orthologue *Lamin C* and used to generate transgenic flies. Wild-type and mutant *Lamin C* was expressed in larval body wall muscles using the Gal4/UAS system. Immunohistochemistry showed that wild-type Lamin C localized to the nuclear periphery as anticipated. In contrast, R264Q caused severe nuclear lobulation and nuclear pore mislocalization. Taken together, these data suggest R264Q disrupts the lamina network, causing other nuclear envelope proteins to mislocalize. Our future directions include analysis of partner proteins that interact with the R264 to determine if a loss of their interaction contributes to nuclear and muscle defects.

351C Conservation of a GAP independent function of the DLC3/Cv-c RhoGAP proteins required for male gonadogenesis

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HIGHLIGHTS:
- *Drosophila* Cv-c RhoGAP null mutations experiment testis dysgenesis akin to human patients with mutations in the homologous DLC3 RhoGAP protein.
-The DLC3/Cv-c male gonadogenesis function is independent of their Rho GAP function and requires a functional START domain.
-Cv-c is required to maintain the germ cell ensheathment in *Drosophila* testis.
- DLC3 rescues testis dysgenesis in *cv-c* null mutants suggesting a deep functional evolutionary conservation.

The DLC3 RhoGAP human protein has been implicated in a case of 46,XY gonadal dysgenesis where two patients inherited a mutation in the START domain, however, no definitive confirmation has been provided yet linking this mutation with male gonadal dysgenesis.
DLC3 belongs to a subfamily of RhoGAP proteins containing three conserved domains: a SAM, a GAP and a START domain. The three domains are also present in the homologous *Drosophila* Cv-c RhoGAP88C protein and DLC3 can functionally substitute for Cv-c. We have previously analysed Cv-c activity in the ectoderm where the GAP domain is absolutely required for its function. However, Cv-c mesodermal requirement has not been analysed yet.
We show Cv-c is specifically expressed and required in the male gonadal mesoderm. *In vivo* analysis of *cv-c* null mutants deleting the GAP and START domains shows normal testis development up to gonad coalescence at st15. However, after st15 the germ cells become extruded from the testis due to their defective ensheathment by mesodermal interstitial gonadal cells, which express lower levels of E-Cad and Neurotactin in the mutants.
Surprisingly, mutants for the *cv-c*^{7} allele, a point mutation only lacking a functional GAP domain, have normal testis. We also find Rho1 mutations do not normalize *cv-c* null mutations indicating a novel Rho GAP independent function in the gonad.
Expression of Cv-c protein variants lacking a functional GAP domain can rescue testis development but not mutants lacking the START domain. Interestingly, human DLC3 can partially rescue *cv-c* null gonad defects but not the DLC3 START mutant allele present in the human patients.
Our results show a new Rho GAP independent specific function for this protein family that is required for testis development and has a deep evolutionary conservation.

352A The oncoproteins H3 K27M and EZHIP inhibit PRC2 by conserved mechanisms in mammals and *Drosophila melanogaster*

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Central nervous system (CNS) tumors are the leading cause of solid tumor death in children. Among the deadliest and most common pediatric brain tumors are diffuse intrinsic pontine glioma (DIPG) and posterior fossa ependymoma type A (PFA). Most DIPG tumors harbor a lysine-to-methionine mutation at residue 27 on histone H3 (H3 K27M). Nearly all PFA tumors feature elevated expression of the previously uncharacterized protein EZHIP. These tumors arise from different cell types and harbor distinct molecular drivers but share remarkable similarities, including a near-complete loss of histone H3 trimethylation at lysine 27 (H3K27me3), a mark that contributes to transcriptionally silent chromatin. We have previously shown that H3 K27M and EZHIP are potent inhibitors of the H3K27me3 histone methyltransferase Polycomb repressive complex 2 (PRC2) in