Disruption of Imprinting and Abnormal Growth in Hybrids

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Disruption of Imprinting and Abnormal Growth in Hybrid Mammals
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**Parent-of-origin growth effects**

- Abnormal growth patterns in hybrids are often parent-of-origin specific, such as mules (large, female horse x male donkey) and hinnies (small, female donkey x male horse). This is thought to be caused by a dosage imbalance of growth related genes.

**Dwarf Hamster as a Model System**

- Normal sized embryo and placenta
- Large hybrid
- Overgrown embryo and placenta

**Methods: Testing for Differential Methylation Patterns Between Hybrid hamsters and Parent Species**

**Candidate Gene Search**
- Searched literature on all disrupted imprinted genes for evidence of CpG islands in other species
- Aligned gene sequences to find conserved regions for primer design

**Lab Work**
- Extracted DNA from placental tissue of parent species and reciprocal hybrids
- Treated extracted genomic DNA with sodium bisulfite to convert non-methylated 'C's to 'T's
- Designed primers to isolate desired CpG island regions
- Amplified region using PCR

**Analysis**
- Aligned sequencing reads of parent species and hybrids to compare differences in methylation status at specific sites (in progress)

**Disrupted Imprinting in Hybrids**

- Imprinting causes allele specific expression. 69 of 88 imprinted genes show disrupted expression in hybrid hamsters relative to parent species.

**Allele-Specific DNA Methylation**

- When a 'C' is followed by a 'G' in the genome, it may be methylated. Clusters of methylated 'C's are called CpG islands. These can alter gene expression levels.

**Implications**

- Molecular mechanisms that regulate development may play an important role in mammalian species formation. Imprinting regulation may contribute to postzygotic barriers that lead to speciation.

**Genome Evolution and Speciation**

- Many of these genes are also found to be miss expressed in various types of cancer. Hybrid growth patterns are very similar to those found in rare but serious growth-related birth defects in humans, such as Beckwith-Wiedeman Syndrome.

**Results/Conclusions**

- Studying DNA methylation in a non-model species faces many challenges. Nonetheless, my initial results have found several CpG islands around candidate genes that may control imprinting, and I have successfully designed primers for two of these so far.

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