DMDD consortium

The DMDD consortium brings together scientists from across the UK developmental biology community, involving seven research centres and with leading researchers in virtually every facet of mammalian embryo development.

Similar projects around the world

DMDD is the UK part of a worldwide effort coordinated by the International Mouse Phenotyping Consortium (IMPC).

Similar work is already underway at the Toronto Centre for Phenogenomics - more will soon start in the USA, France and Japan.

NEW DMDD WEBSITE

Sharing data lies at the heart of the DMDD programme. The new website (www.dmdd.org.uk) brings all the data from DMDD research into a single place, freely available to the scientific community.

With a modern, easy-to-navigate interface, the new site integrates all the different types of data and incorporates powerful search functions, providing:

- access to all image data, viewable up to full resolution
- interactive tools for image navigation
- standardised phenotype annotations
- phenotypes viewable by embryo and mutant lines
- searchable by gene and phenotype
- phenotype terms link directly to images where the phenotype is highlighted
- linked orthogonal views enable dynamic exploration of data
High resolution episcopic microscopy (HREM) is used in the DMDD programme because it offers the combination of simplicity and unrivalled resolution for 3D analysis of embryos. Up until now, no commercial HREM apparatus has been available, however this is now set to change.

Following a collaboration with DMDD researchers at the Francis Crick Institute Mill Hill Laboratory (formerly MRC National Institute for Medical Research), Indigo Scientific now offers a dedicated HREM apparatus which includes a workstation and custom software.

**STATISTICS**

- **Mutant lines studied:** 71
- **Embryos:** 239
- **HREM images:** 1,715,483
- **Mutant lines analysed for HREM &/or placenta:** 48
- **Embryos analysed:** 110
- **HREM images:** 723,279
- **Total images on website:** 3,937,109

**PUBLICATION**

Weninger, WJ; Geyer, SH; Martineau, A; Galli, A; Adams, DJ; Wilson, R and Mohun, TJ (2014) Phenotyping structural abnormalities in mouse embryos using high resolution episcopic microscopy. *Disease Models & Mechanisms* 7, 1143-1152
We also want to see which aspects of the placental defects can be recapitulated in vitro. We are currently using CRISPR technology to knockout the same three factors in trophoblast stem cells. The method is so quick and efficient that we are hoping to extend the study to 10 genes from the mid-gestation lethal cohort. We can test how well the knockout stem cells self renew and proliferate. We can also see whether their ability to differentiate into different placental cell types has been affected by the mutation.

Myriam Hemberger

H&E sections show a dramatic reduction in allantoic blood vessels in the chorionic ectoderm of the Crb2 mutant placenta.

Myriam and her colleagues are studying three conditional gene deletion lines (Crb2, Nubp1 and Bap1) to see if the presence of a wild type placenta rescues or ameliorates any part of their embryonic phenotype.

Myriam Hemberger

We have found that almost 70% of mid-gestational lethals have a severe defect in extra embryonic development. These numbers exceed even our most generous projections from the current literature, and underpin the notion that the impact of gene mutations on placental development has been vastly underestimated.

Myriam Hemberger
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