Institut für Experimentelle Genetik, IEG

Helmholtz Zentrum München
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Model for Human Disease

Themen Schwerpunkte

1. Diabetes
2. Knochen-/Knochenerkrankungen
3. Modell der embryonalen Entwicklung (Fokus: Notch-Signalweg)

BONE & CARTILAGE DISEASES

<table>
<thead>
<tr>
<th>Patterning</th>
<th>Growth</th>
<th>Remodeling</th>
<th>Immune system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polydactyly</td>
<td>Osteogenesis imperfecta</td>
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</tbody>
</table>
| ALI3, ALI9, 
ALI12, ALI19, 
ALI37 |
| Syndactyly | Osteoporosis |
| ALI6, ALI10, 
ALI27 |
| Osteoarthritis |
| ALI15, ALI14, ALI18 |

Caused by a cryptic splice site in Col1a1

Model for type II OI

Bone phenotype:
- Mineralisation defect
- Bone deformity
- Fractures
- BMC and BMD reduced

Bisphosphonate rescues bone phenotype but not lethality

The Screens

**SYSTEMIC DISEASES**

**Bone phenotype**
- Mineralisation defect
- Bone deformity
- Fractures
- Beaded ribs
- Reduced bone mineral content & decreased bone mineral density

**Systemic effects**
- Lung phenotype
- Heart phenotype
- Reduced fat mass & increased lean mass
- Metabolic alterations

**Gene–environment interactions in Type 2 Diabetes pathogenesis**
- Mouse models

**Type 2 Diabetes**
- Pancreatic β-cell dysfunction (impaired insulin secretion)
- Impaired insulin action

**Experimental mouse models**
- Allow for detailed & accurate phenotyping due to:
  - Environmental factors that can be tightly controlled
  - Genetic diversity can be reduced
  - No limitations in biosamples

**Pathophenotype closely mimicks human polygenic obesity-induced diabetes**
- Hyperglycaemia
- Pancreatic islet atrophy
- Liver steatosis
- Increased serum insulin, leptin, TAG

**Mice with mutations in particular genes to unravel their function in T2D pathogenesis**
Key Activities of IEG

Large-scale genomics approaches:
- Mutant Production (Mouse)
  - Mutagenesis Screens
- Archiving: German node of EMMA
- Phenotypic Characterisation
  - German Mouse Clinic
- Genomics, Transcriptomics and Proteomics
- Data Acquisition and Interpretation
- In silico Functional Genomics

Was wir anbieten:

- Forschungspraktika:
  - Anmeldung zu jeder Zeit
  - Praktikumsdauer 6 Wochen, bis zu 10 CPs
  - Vortrag und Präsentation der Arbeit im Anschluss
    und Praktikum
- Blockpraktikum: Entwicklungsgenetik der Tiere
- Seminare, Journal Clubs (SS)
- Vorlesungen:
  - Entwicklungsgenetik
  - Genomik
- Master/Diplomarbeiten und Promotionen

Blockpraktikum "Entwicklungsgenetik der Tiere" 10 ECTS (mit IDG)
Themes:
- From Genes to Mouse Mutants and their Phenotype Analysis
- Zebrafish Embryology

Tierversuche/Verantwortung
Establishment & Culture of Embryonic Stem Cells
Gene Mutagenesis in Embryonic Stem Cells
Generation of Knockout/Transgenic Mice

Cryoconservation of germ cells and in vitro fertilisation
In vivo Mutagenesis (ENU, Transposons)
Zebrafish Embryology
Zebrafish Embryology

Phenotyping I: Histology
Phenotyping II: Gene expression analysis
Phenotyping III: German Mouse Clinic
Phenotyping IV: Behavioural Analysis

Vorlesung: Entwicklungsgenetik
First week in the life of a mouse
From the gastrula to midgestation
Principles in development
  - How to get "organized"
    "Up and down, Back and Belly, Left and Right": The question of positional
      information.
    lateral inhibition - watch your neighbour!
    epithelial-mesenchymal transformation - The same story everywhere.
  - How to pattern extremities
  - The other side of life – aging
Organogenesis:
  "Get in Shape": Making bones and muscle from somites.
the ectoderm/neuroectoderm and its derivatives
the endoderm and its derivatives
Development of sensory systems:
  visual system,
  auditory system,
  smell, taste and touch
General discussion, social and ethical issues
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