What is Emberger Syndrome (ES)?

Before Symptoms

After Symptoms

White blood cell

Leukemic blast

Red blood cell

Platelet
GATA2 association with ES

Mutation sites

50% active but abnormal
What is the role of **GATA2**?

**Gene Ontology**

- **Cellular Components**
  - Nucleoplasm
- **Molecular Functions**
  - Zinc Ion Binding
  - Transcription Factor Binding
- **Biological Process**
  - Hemostasis
  - Regulation of body fluid levels
How well conserved is GATA2?

- Human: 99%
- Chimpanzee: 99%
- Mouse: 88%
- Drosophila: 74%
- Zebrafish: 71%
- Arabidopsis: 31%
GATA2 across species

Model Organism:

Average distance using PID
Goal: To understand the pathology underlying Embberger Syndrome and GATA2 haploinsufficiency.

What is the relationship between GATA2 and ES?
Hypothesis: Mutations in $GATA2$ regulate genes that affect the function of hematopoietic stem cells.

Aim 1: Identify proteins that interact with $GATA2$

Aim 2: Identify interacting proteins that are differentially expressed in mutant mice

Aim 3: Determine if $GATA2$ interacting proteins cause ES phenotypes
Aim 1: Identify proteins that interact with Gata2 that regulate hematopoietic function

Approach:

STRING database
Aim 1: Identify proteins that interact with Gata2 that regulate hematopoietic function.
Aim 2: Identify **GATA2** interacting proteins that are differentially expressed in mutant mice

**Approach:** RNA Sequencing

**Predicted Results:**

- **WT GATA2**
- **Mutant GATA2**
Aim 3: Determine if differentially expressed interacting proteins cause ES phenotypes

Approach: CRISPR/Cas9 Knockout

ES Phenotypes: Lymphedema & high myeloblast count
**Aim 3**: Determine if differentially expressed interacting proteins cause ES phenotypes

**Predicted Results:**

<table>
<thead>
<tr>
<th>Function of gene</th>
<th>Wild Type</th>
<th>Wild Type Knockout</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematopoiesis</td>
<td>Normal myeloblast count</td>
<td>Abnormal myeloblast count</td>
</tr>
<tr>
<td>Lymphatic System Development</td>
<td>No Lymphedema</td>
<td>Lymphedema</td>
</tr>
</tbody>
</table>
Future Directions

Target-based

Overexpression of a protein of interest

\[ \downarrow \text{Add compounds} \]

Screen for compounds that bind/modulate protein function

\[ \downarrow \text{Add compounds to cells/organisms} \]

Assay for phenotypic outcome

Chemical Genetics

![Chemical Structures](image)

A
B
C
D
References

Images

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Articles


Questions?