Induction of IL-10 producing NK cells and their role in protection from cerebral malaria

Cassaundra Burt

T35 Medical Student Summer Research Program
Jameson Lab
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- Plasmodium parasite
- Over 200 million cases worldwide
- ~500,000 fatal cases
- Cerebral malaria (CM)
  - children ≤5 years old in sub-Saharan Africa
  - Fatal 10-30% cases or cause long term neurological sequelae


**Confirmed malaria cases per 1000 population**

- >100
- 50–100
- 10–50
- 1–10
- 0.1–1
- 0–0.1
- No ongoing malaria transmission
- Not applicable

Source: National malaria control programme reports
IL-2 and IL-15 cytokine complexes


IL-15C-treated NK cells are sufficient to protect against CM and induce IL-10 expression

n = 7-15 mice/group  *** P = 0.0005

Kristina Burrack and Sara Hamilton
What signals are needed to induce IL-10 expression \textit{in vitro}?

**Harvest spleens from IL-10-GFP or C57BL/6 mice**

\[\text{→} \quad \text{Sprenocytes or enriched NK cells} \quad \text{→} \quad \text{Culture with IL-15C, IL-2C, IL-2 or media} \quad \text{48h} \quad \text{→} \quad \text{(Add IL-12)} \quad \text{24h} \quad \text{→} \quad \text{Harvest}\]

**NK Cells**

**Splenocytes**

- IL-15C + IL-12
- IL-15C
- IL-2C + IL-12
- IL-2 + IL-12
- IL-12
- IL-15C + IL-12 (B6 control)

**Graph:**

- **IL-10 (ng/mL):**
  - Media
  - IL-15C
  - IL-15C + IL-12
  - IL-2 + IL-12
  - B6 IL-15C/IL-12

- **MFI:**
  - IL-15C
  - IL-2C/IL-12
  - IL-2XIL-12
  - IL-12
  - B6 IL-15C/IL-12

- **n \geq 3**
Conclusions:

1. IL-12 is necessary to induce NK cell IL-10 expression \textit{in vitro}

2. IL-12 may be sufficient to induce NK cell IL-10 expression in a splenocyte environment \textit{in vitro}

3. No significant difference between the ability of IL-2C + IL-12 and IL-15C + IL-12 to induce IL-10-GFP expression \textit{in vitro}
Future Directions:

1. Perform an adoptive transfer of IL-10 expressing NK cells from *in vitro* culture to determine if they protect against CM

2. Further investigate the role of IL-12 in producing IL-10 expressing NK cells

3. Ongoing study to determine if NK cells from mice infected with *Listeria monocytogenes* (LM) and mouse cytomegalovirus (MCMV) can help protect against CM and if they have a similar phenotype to IL-15C treated NK cells
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Questions?