Surviving the crash: mechanisms regulating T-cell number

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Controlling number in the mature T-cell compartment

Division & Differentiation → Effectors → 90% → Death

Quiescent → Survivors
• Heterogeneity associated with the immune response
  – Interactions between molecules regulating cell death and survival

• Spatial and temporal elements
  – Cellular sites for the integration of cell death and survival cues
  – Spatial regulation of Notch activity for cell survival
Cell survival is determined by the availability and uptake of nutrients.
Apoptotic T-cells

wildtype

Bax active -6A7
Nucleus – H33342
The formation of higher order apoptotic structures at the mitochondrion precedes cellular collapse.

Apoptotic T-cells

wildtype

Bax active -6A7
Nucleus – H33342

20.00 min

Tracking bax multimerization at mitochondria
Molecules promoting survival intersect with these events

Notch activity protects from cell death
Molecules promoting survival intersect with these events

Notch activity protects from cell death

Analysis of Bax dynamics by Fluorescence Correlation Spectroscopy (FCS)
Molecules promoting survival intersect with these events

Notch activity protects from cell death

Analysis of Bax dynamics by Fluorescence Correlation Spectroscopy (FCS)

The mitochondrion is a key site for the integration of cell death and survival cues.
The mitochondrion is a key site for the integration of cell death and survival cues.
Notch activity requires the mitochondrial remodeling machinery

Block mitochondrial fusion

control

Percent Apoptotic Nuclei

<table>
<thead>
<tr>
<th></th>
<th>Bax-GFP+STS</th>
<th>Bax-GFP+C6-NIC+STS</th>
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<tbody>
<tr>
<td>scrambled</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Mfn-2 siRNA</td>
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