Summary
Conclusions

Role of AIF in T cell death

A) Low levels of AIF in T cells leads to protection from TSWD, suggesting a pro-apoptotic role of AIF.

B) Enhanced AICD in Hq T cell blasts suggest an anti-apoptotic role for AIF.

C) TSWD is governed by intrinsic pathway with lower caspase-9 activation in Hq T cell blasts.

D) Other mitochondria mediated stress and ER stress mediated death is similar in WT and Hq T cell blasts.

E) AICD is mediated by extrinsic pathway with higher caspase-8 activation and is mediated by higher Fas-FasL, Tnf-α and ROS playing a supportive role in higher cell death in Hq T cell blast.

F) Hq T cell blasts are more susceptible to superoxides and peroxides.

G) Higher death in AICD is rescued by ROC quencher and SOD mimic EUK-134, suggesting peroxide scavenger role played by AIF in T cells.

Affect of AIF hypomorphism on peripheral immune compartment and T cell development

A) Hq mice show reduction in frequencies and numbers of peripheral T cells while B cell compartment remains unaffected suggesting defect to be T cell specific.
Summary

B) Higher frequency of activated and memory T cell were found in peripheral T cell pool and naïve T cell numbers and frequencies were drastically reduced in Hq mice.

C) Rate of proliferation in vitro was not drastically different between WT and Hq T cells.

D) Thymus is hypocellular in Hq mice.

E) Reduction in number and frequencies of DP and SP cells is seen in Hq mice.

F) Thymic development block is seen in DN3a to DN3b transition, with a higher frequency of DN3 cells showing annexin v positivity.

G) Higher death is also seen in DN4 and DP stages of development.

H) Higher ROS is seen as a primary cause of cell death during T cell development.

I) Hypocellularity is rescued on a 14 day treatment with SOD mimic and ROS quencher EUK-134, suggesting AIF to be playing a ROS quenching role in various stages of T cell development.

J) Using in vitro T cell development cultures we established that, absence of AIF in T cells was the primary cause for the developmental block.