

Leptin promotes B cell response in autoimmune arthritis

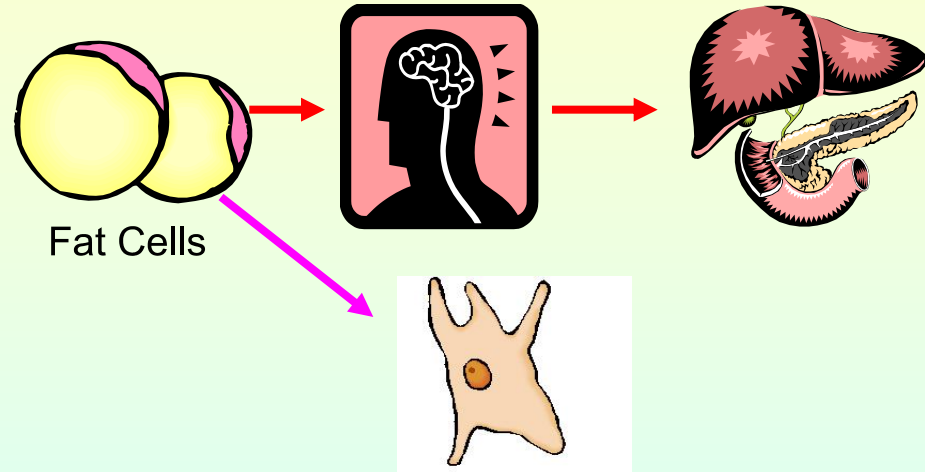
Liwei Lu

University of Hong Kong, China

Leptin

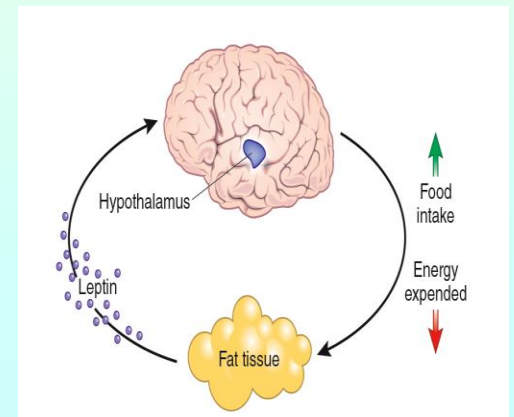
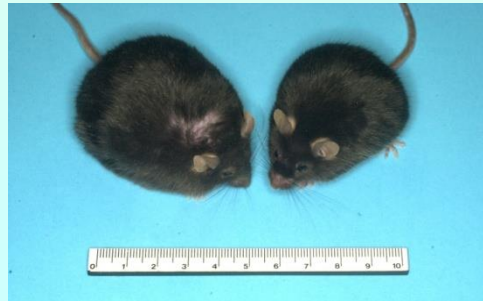


Jeffrey Friedman

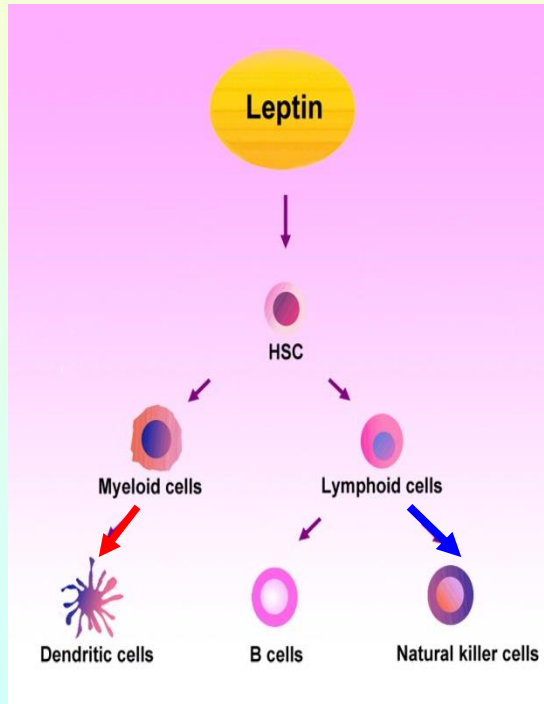


Douglas Coleman

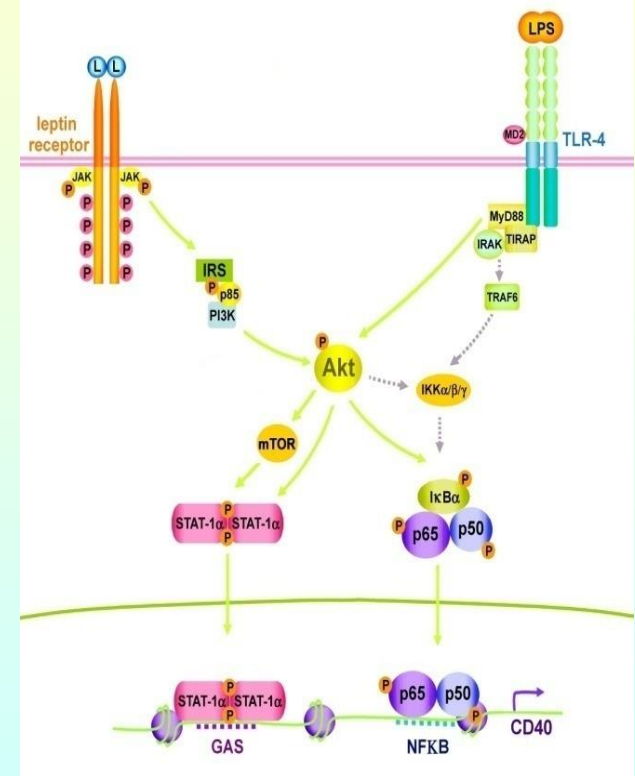
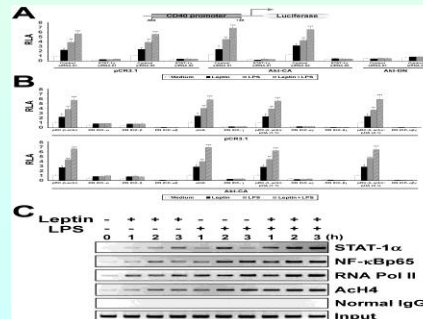
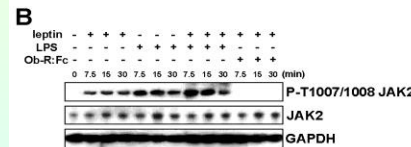
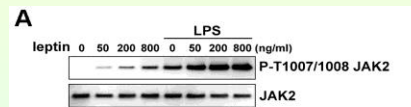
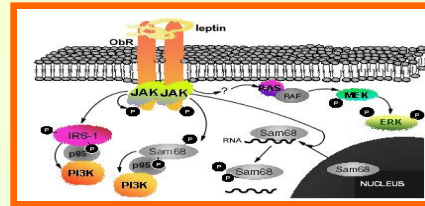
Db/db mice



Leptin regulates DC/NK maturation via activation of Akt pathway

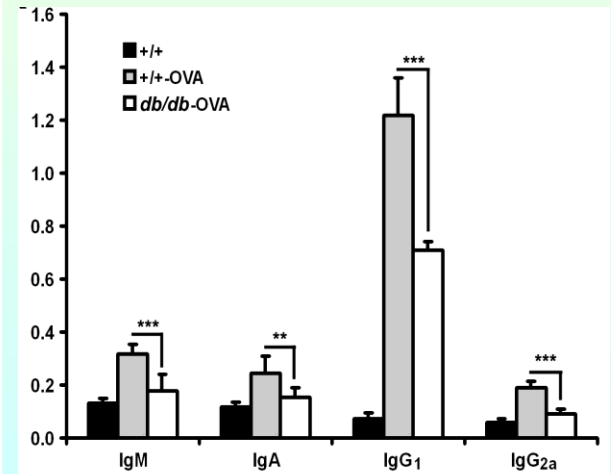
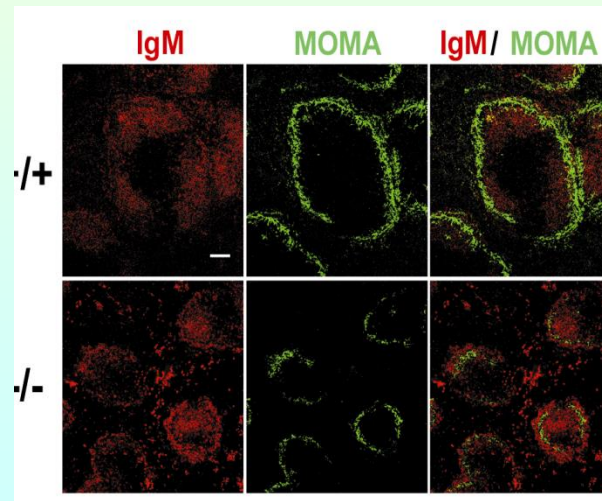
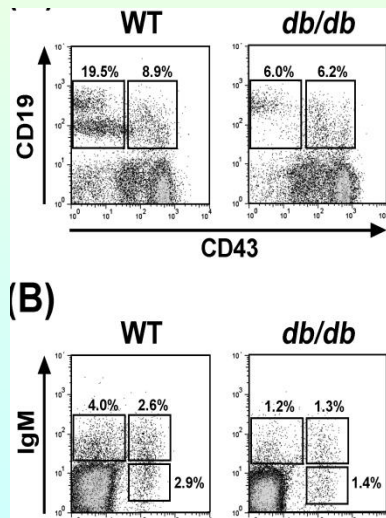
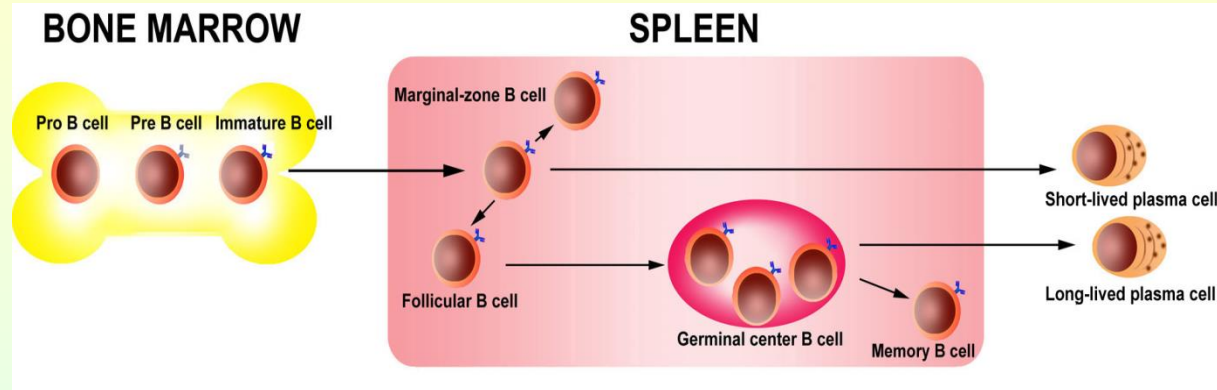


Leptin activates JAK/Stat



Lam Q, et al, *JBC* (2008)
 Lam Q, et al, *EJI* (2006)
 Lo C et al, *CMI* (2007)
 Lam Q & Lu L, *CMI* (2008)

Leptin regulates B cell maturation and function

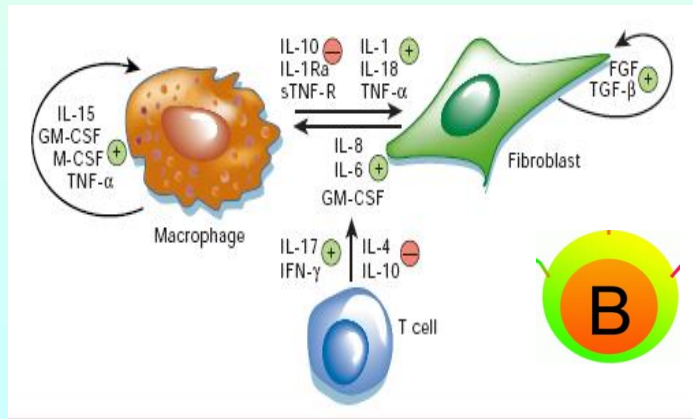
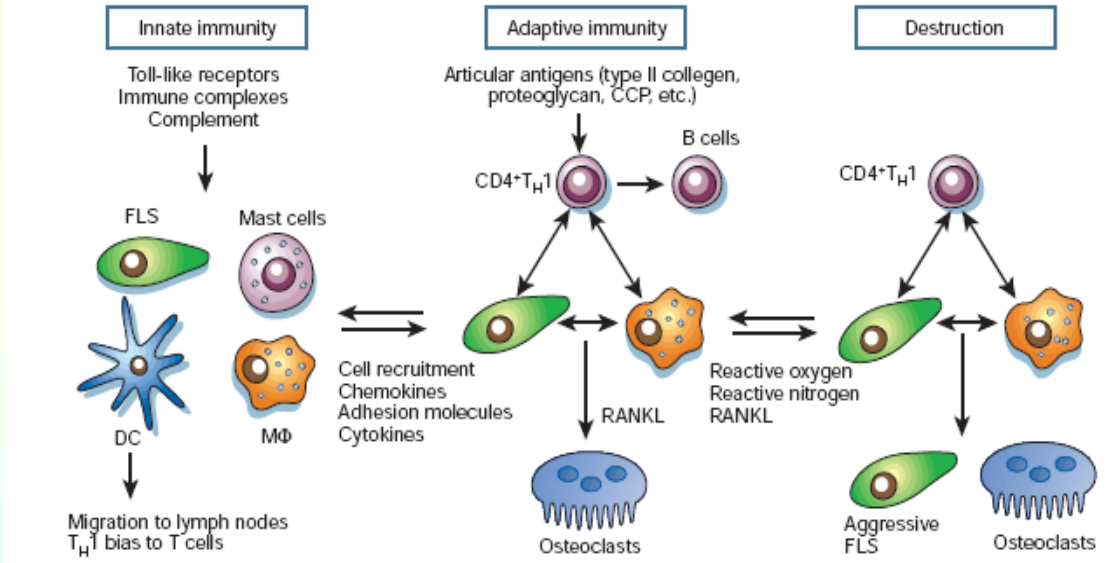


Lam Q et al, PNAS USA (2010)

The Immunopathogenesis of Rheumatoid Arthritis

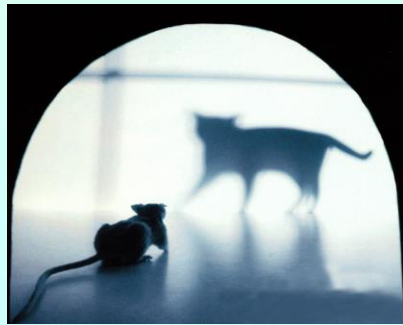


insight review articles
 Evolving concepts
 of rheumatoid arthritis
 Nature (2003)
 Gary S. Firestein

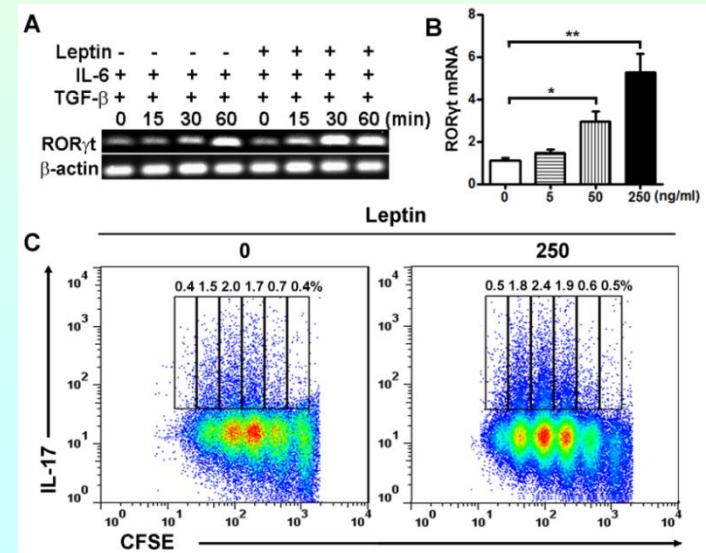
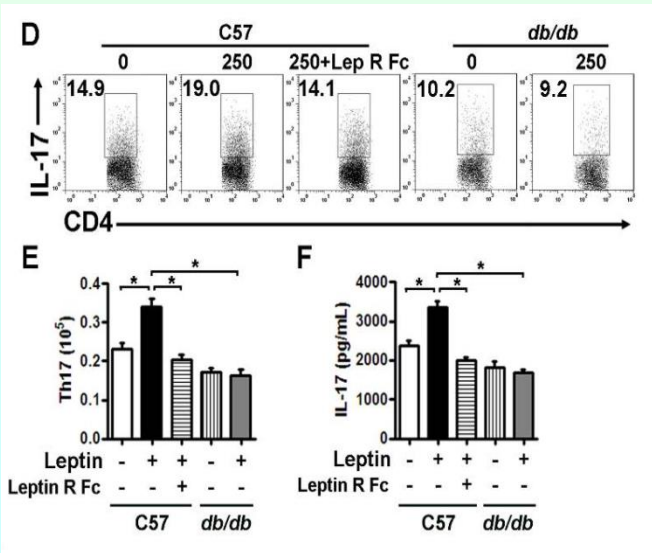
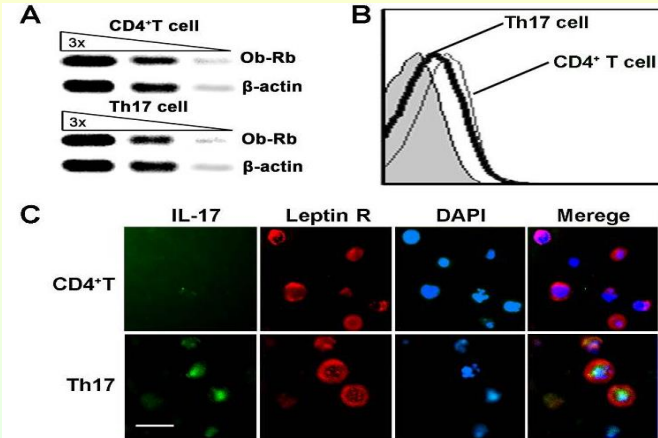
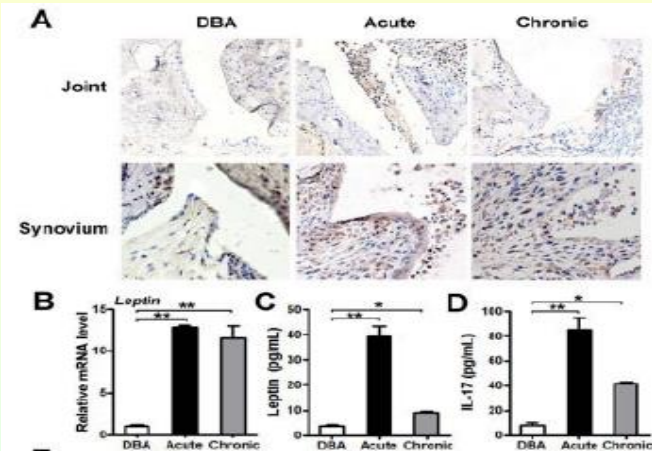


Friend or foe in RA?

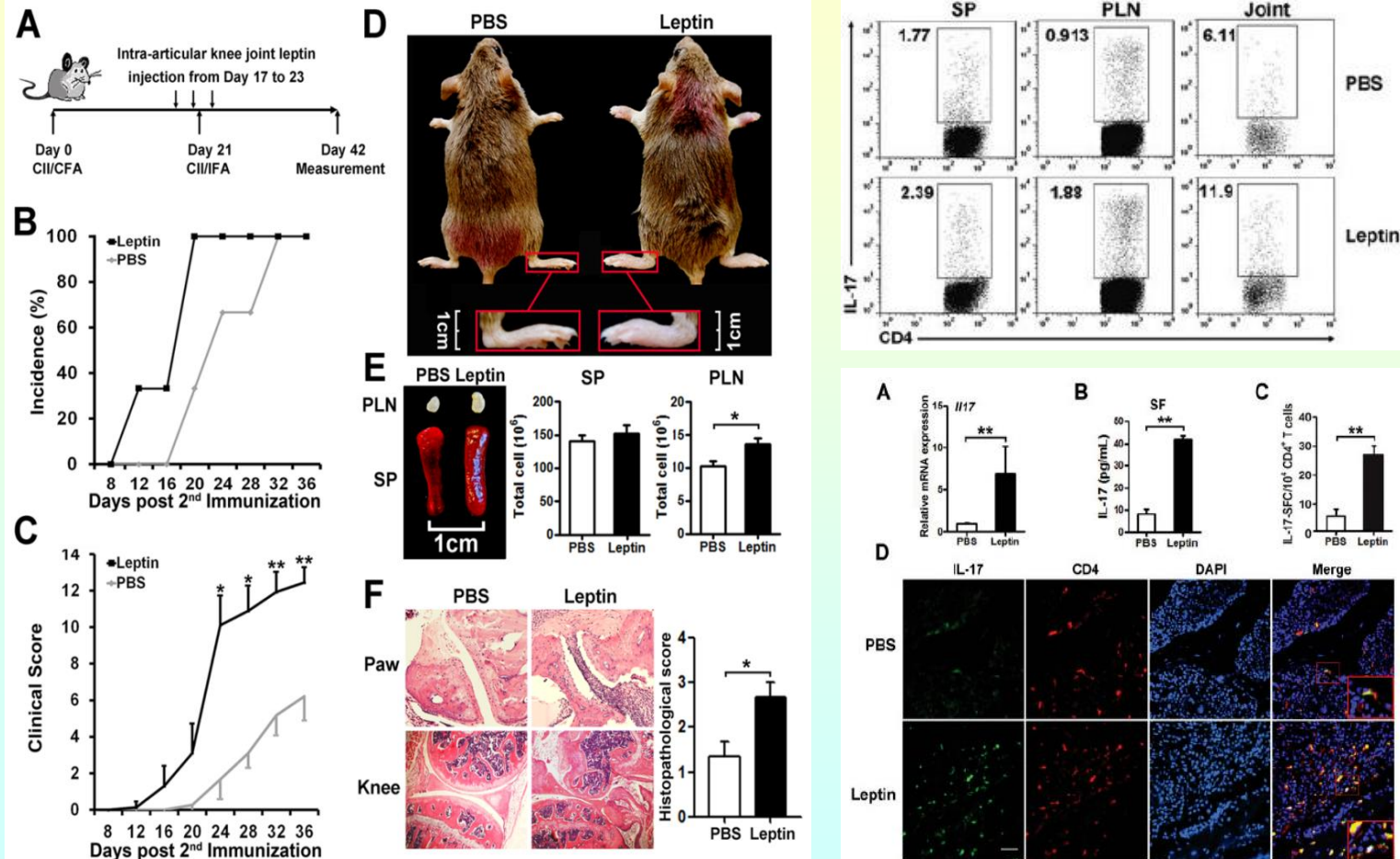
Leptin
 →
 ?



Leptin promotes Th17 cell differentiation



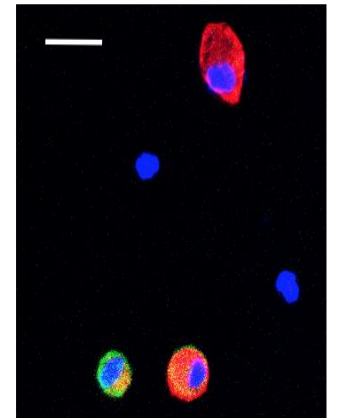
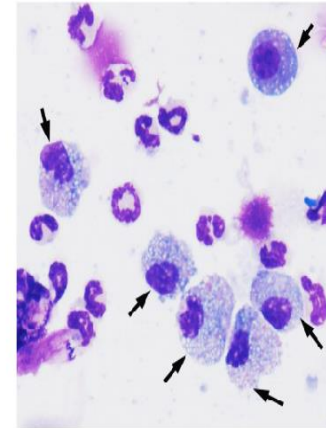
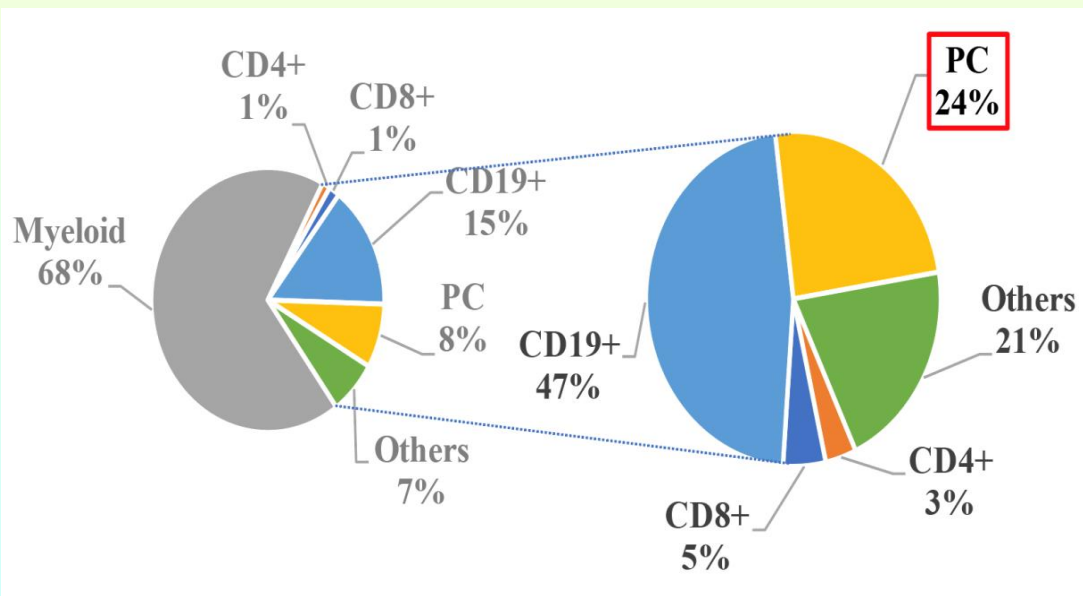
Leptin injection drives T cell response and CIA progression



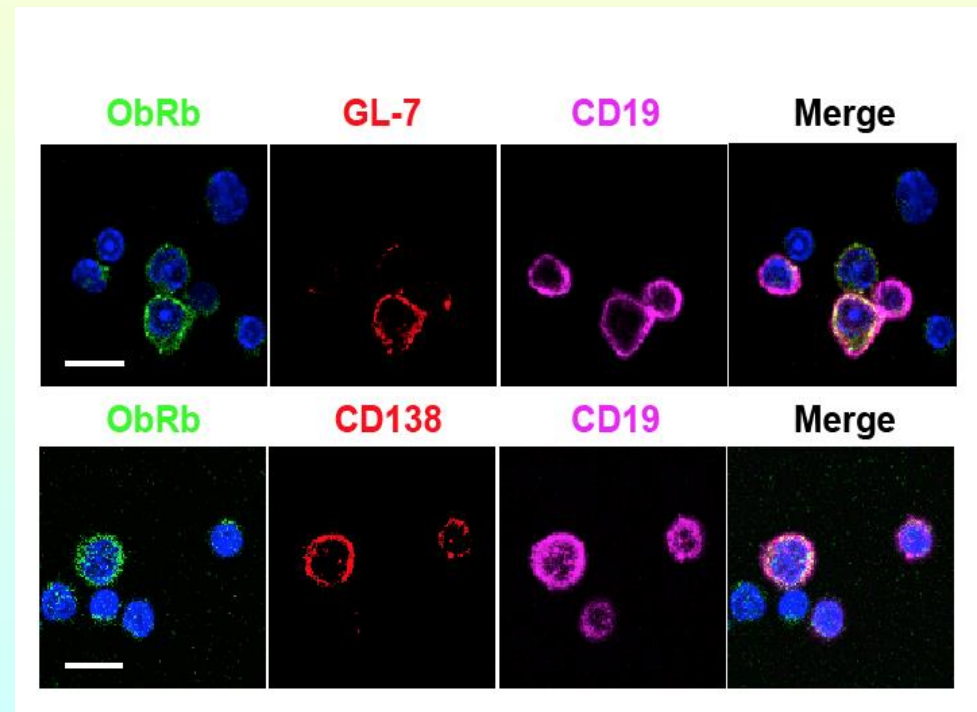
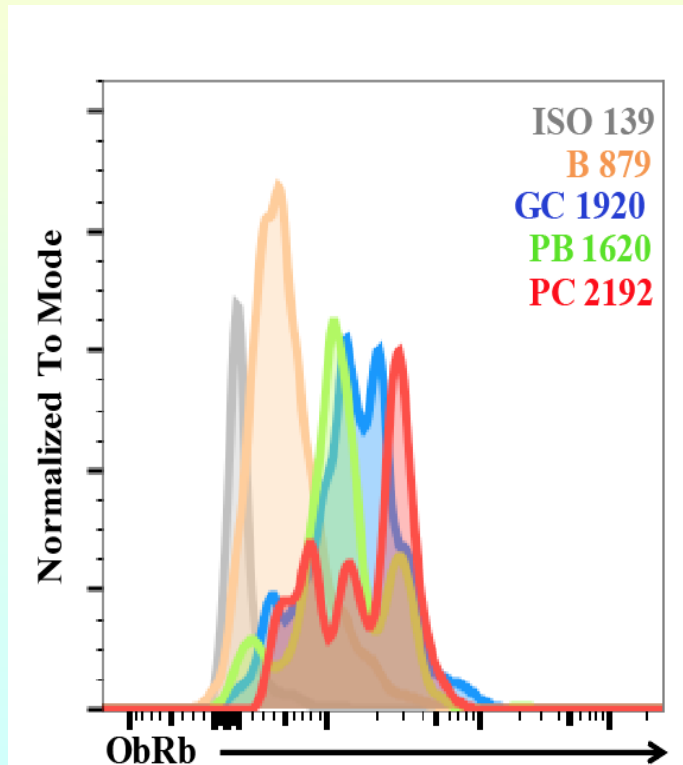
Deng J et al, A&R (2012)

How does leptin regulate B cell response in CIA?

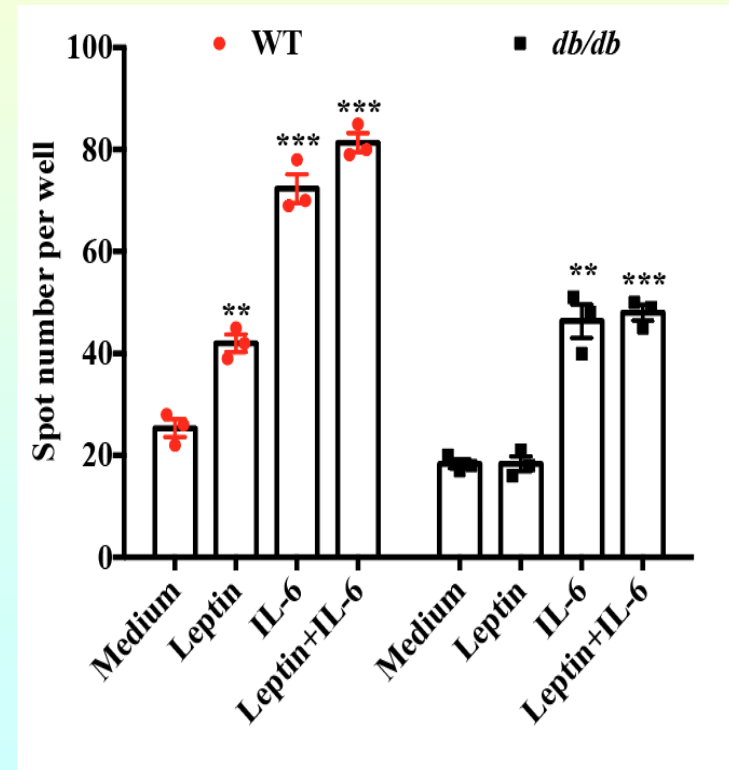
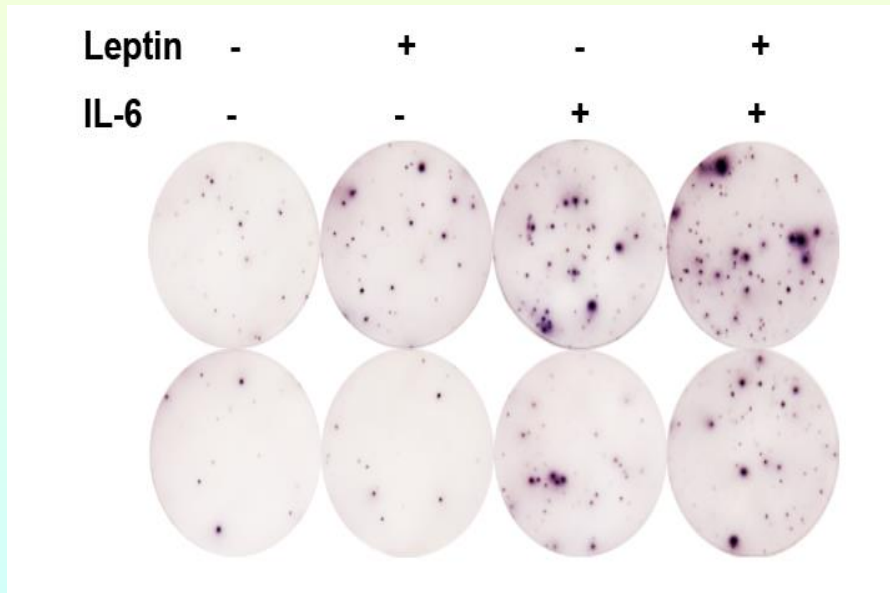
CI1-specific PCs enriched in CIA synovial fluid



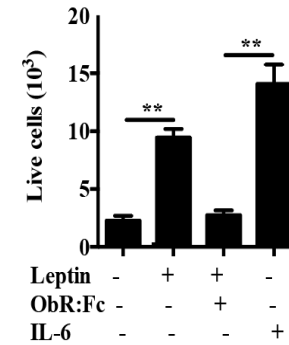
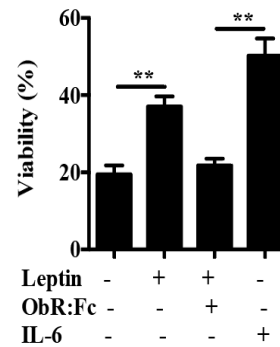
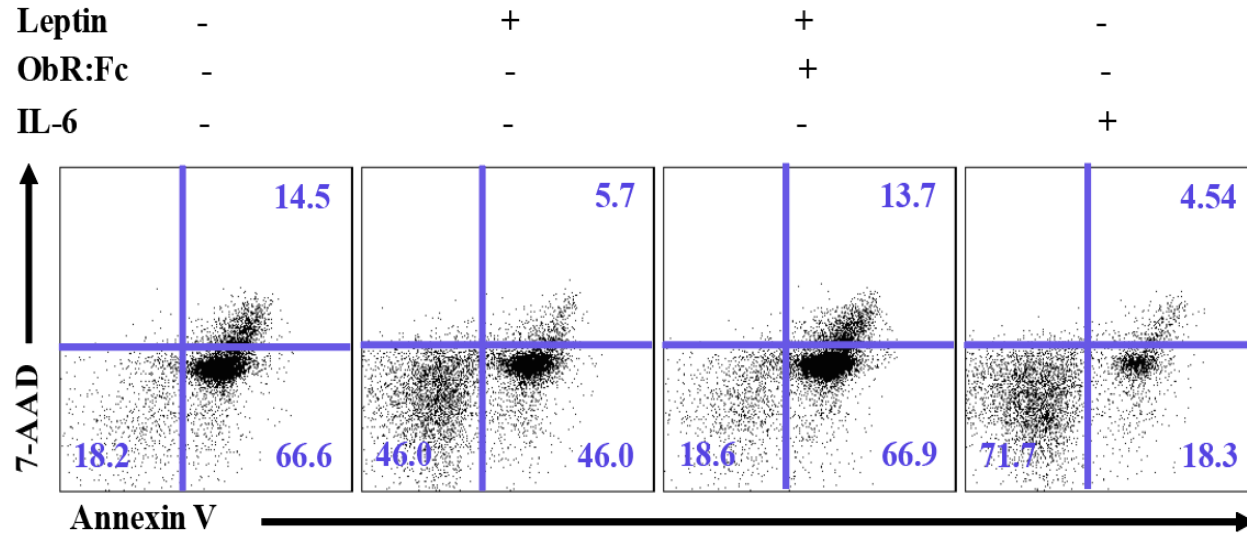
Plasma cells express high levels of leptin receptor



Leptin promotes Ab production by PCs

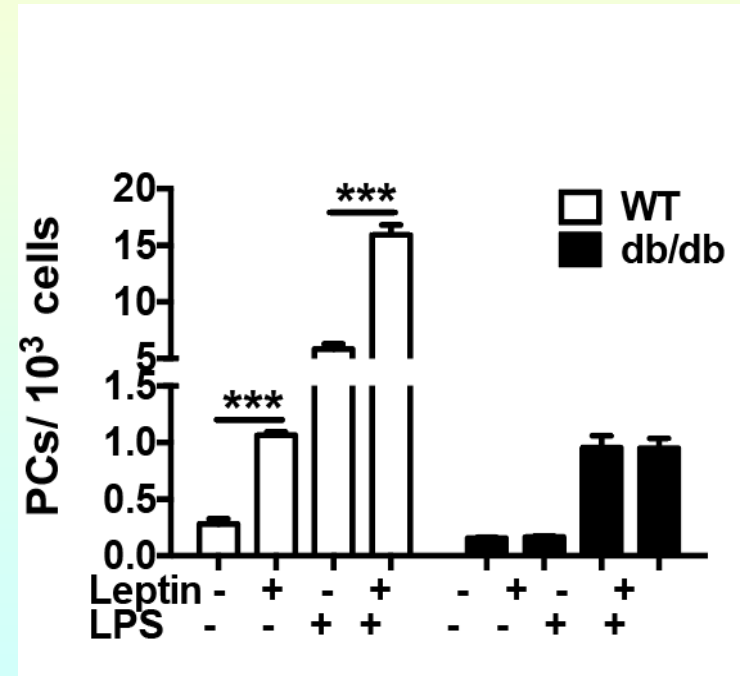
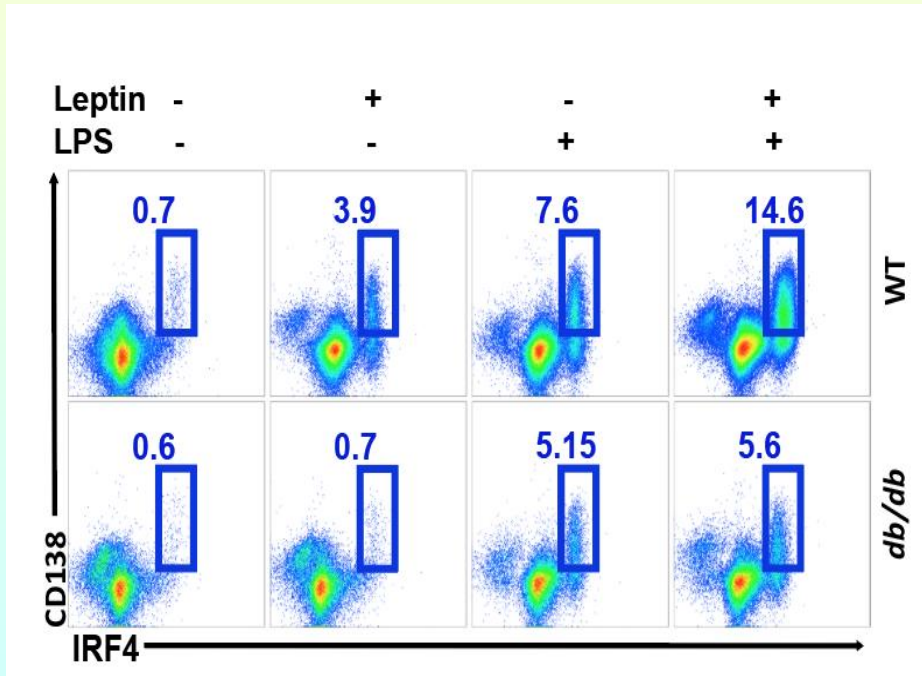


Leptin promotes PCs survival in culture

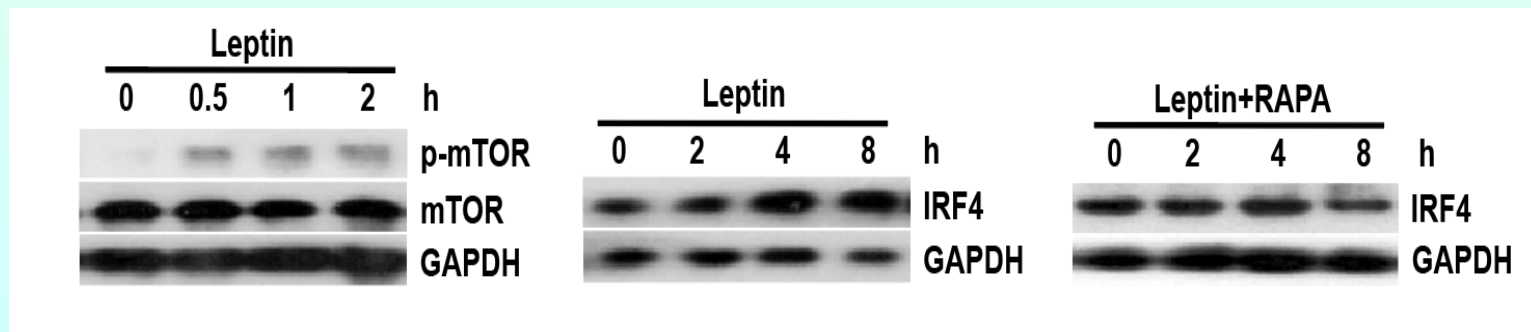
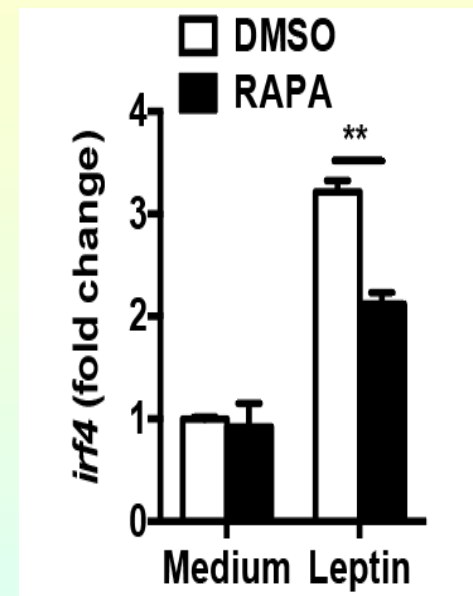
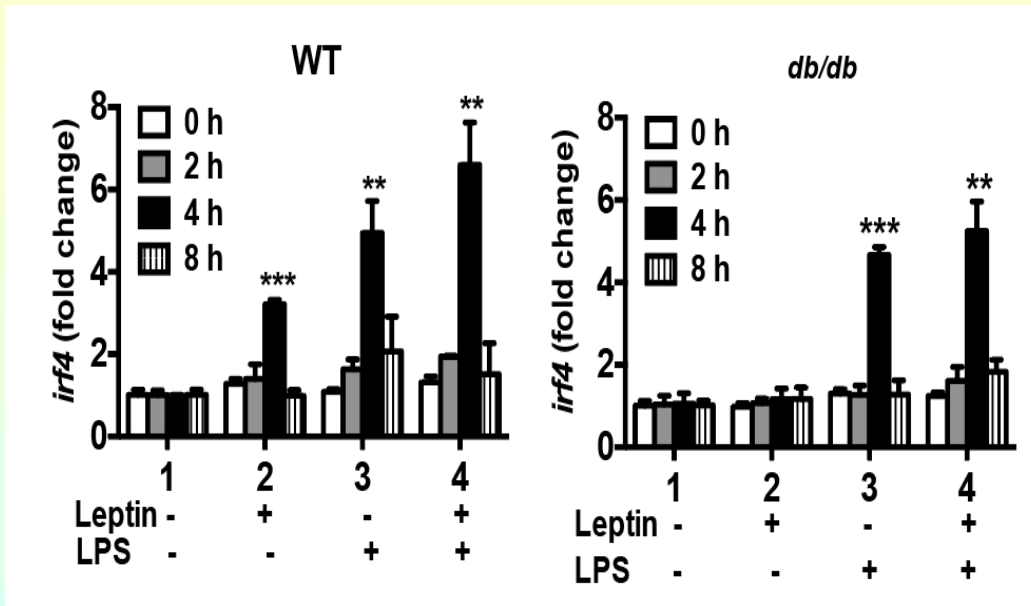


Leptin promotes PC differentiation in culture

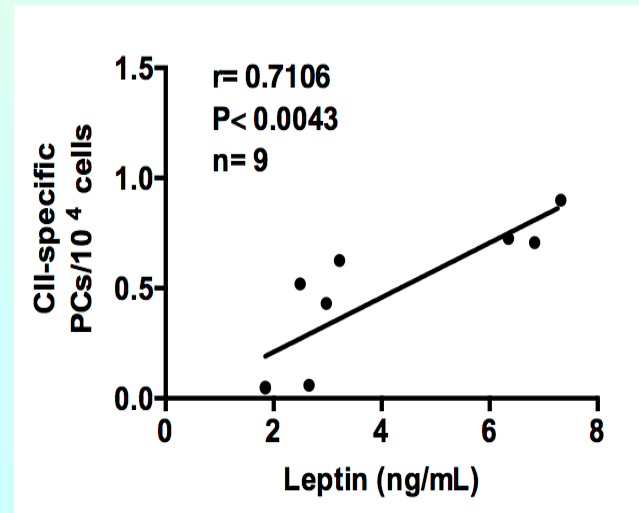
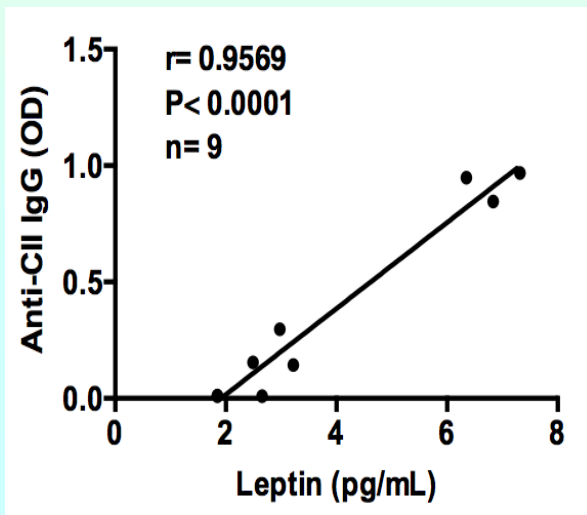
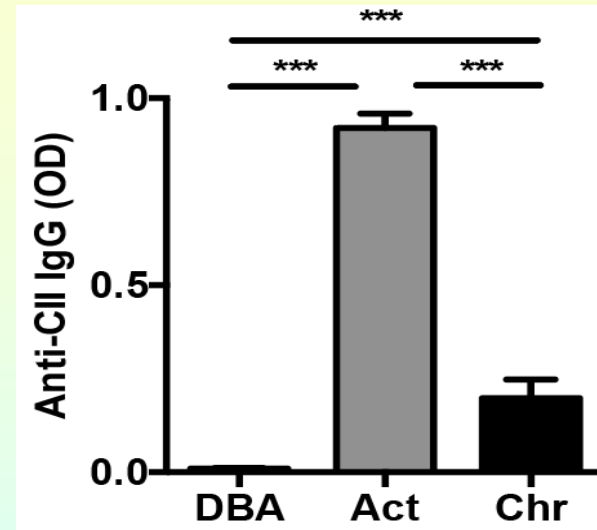
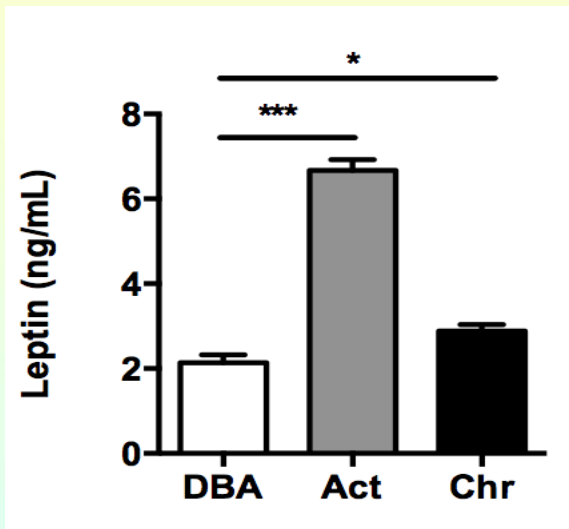
GC B cell culture



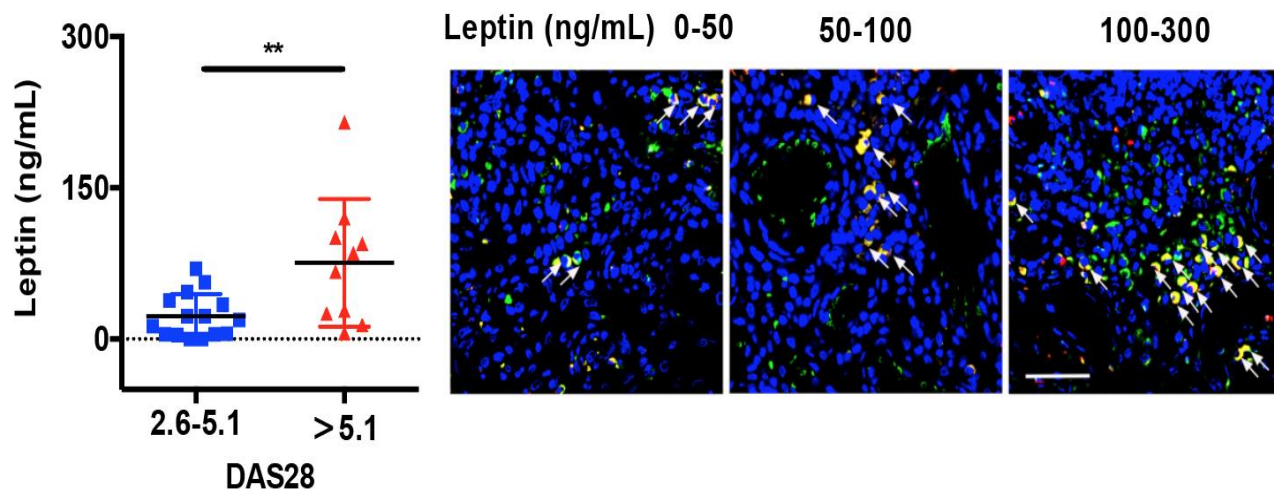
ObR-mTOR-IRF4 axis mediates PC response



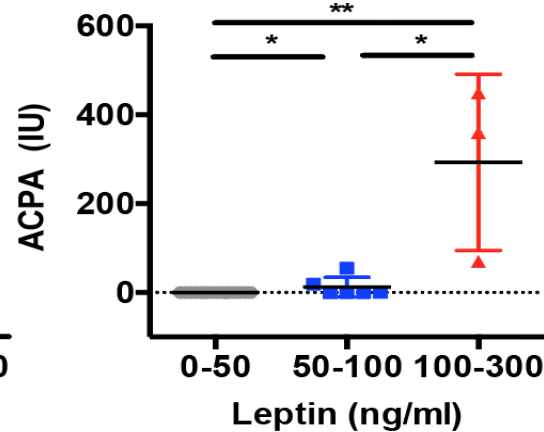
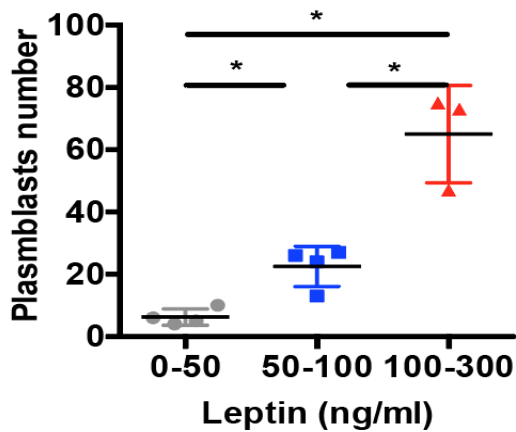
Leptin levels correlate with autoAbs in CIA



Synovial leptin correlates with disease activities in RA patients

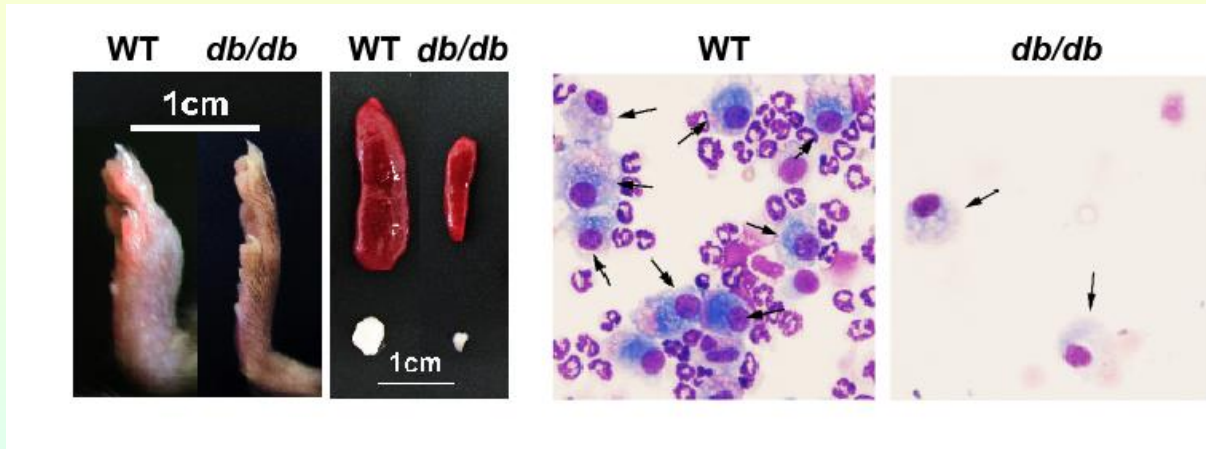


Leptin levels vs AutoAbs

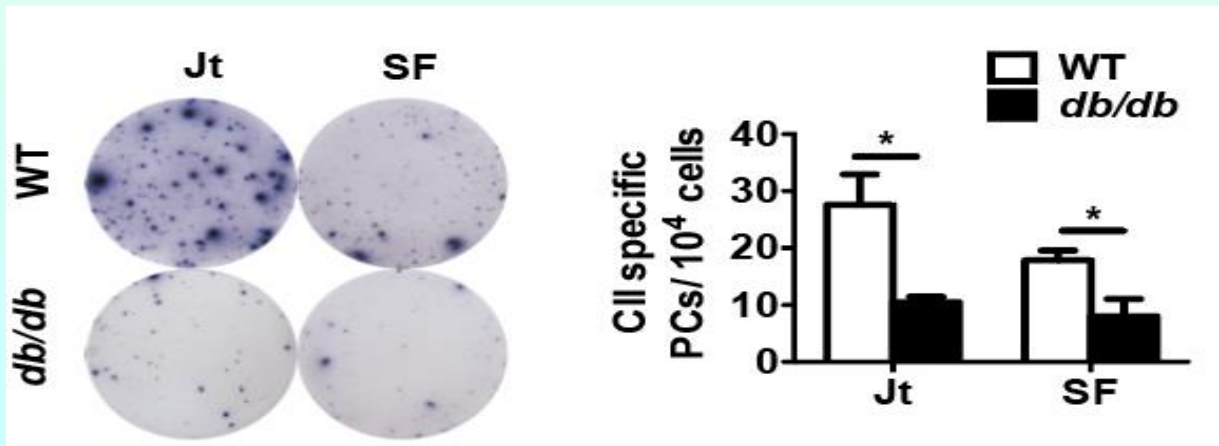


Leptin receptor deficiency impairs plasma cell response

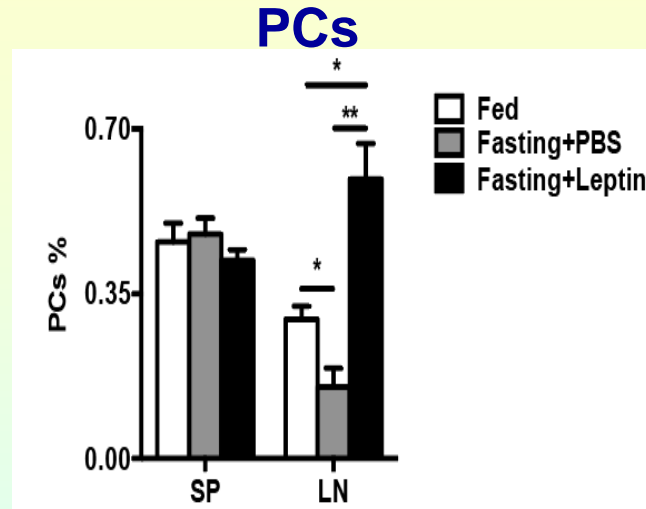
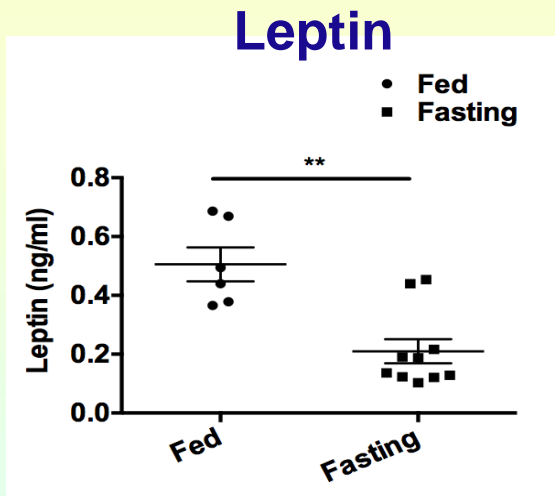
Reduced PCs in db/db mice



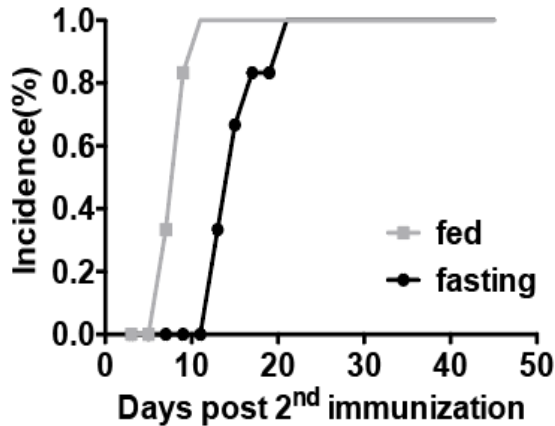
Reduced CII-specific PCs in joints of db/db mice



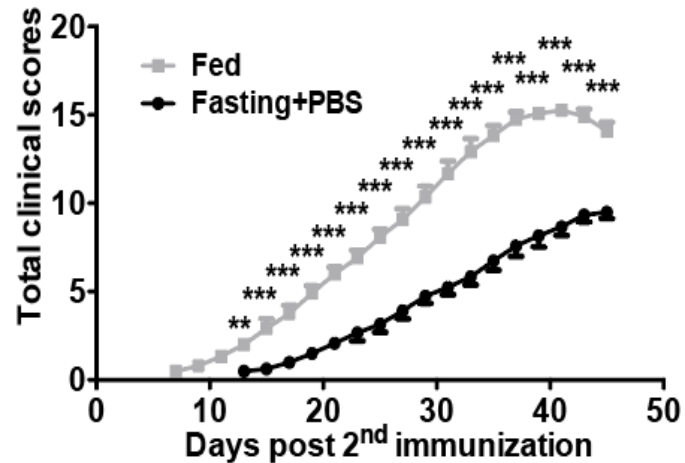
Fasting suppresses CIA development



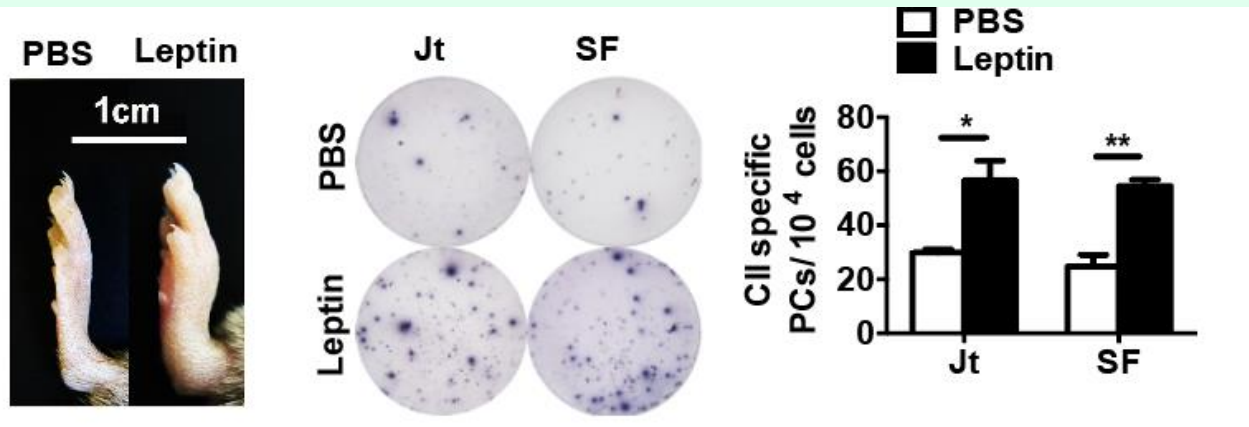
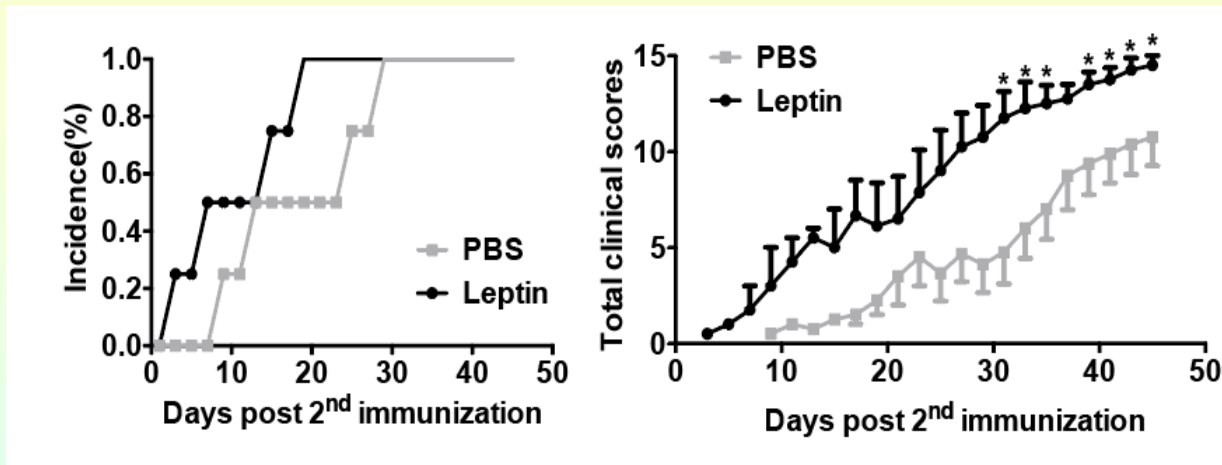
CIA onset



Disease severity

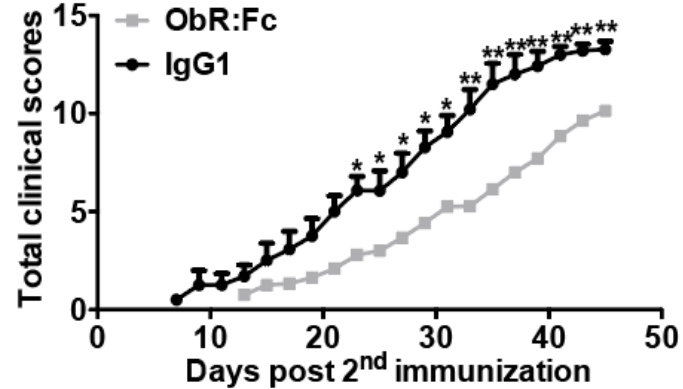
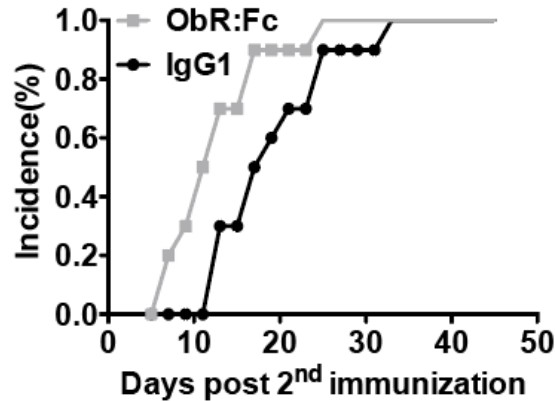


Leptin intraarticular injection exacerbates CIA

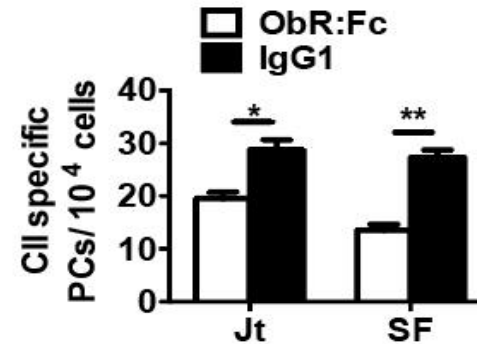
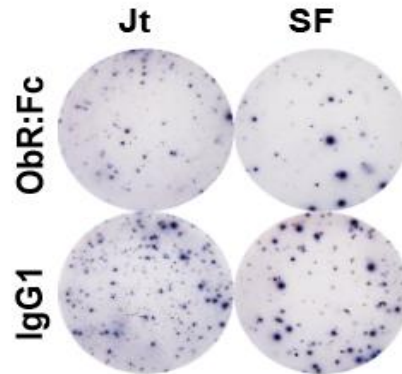


Leptin blockade ameliorates CIA progression

ObR:Fc---- Leptin receptor blocker

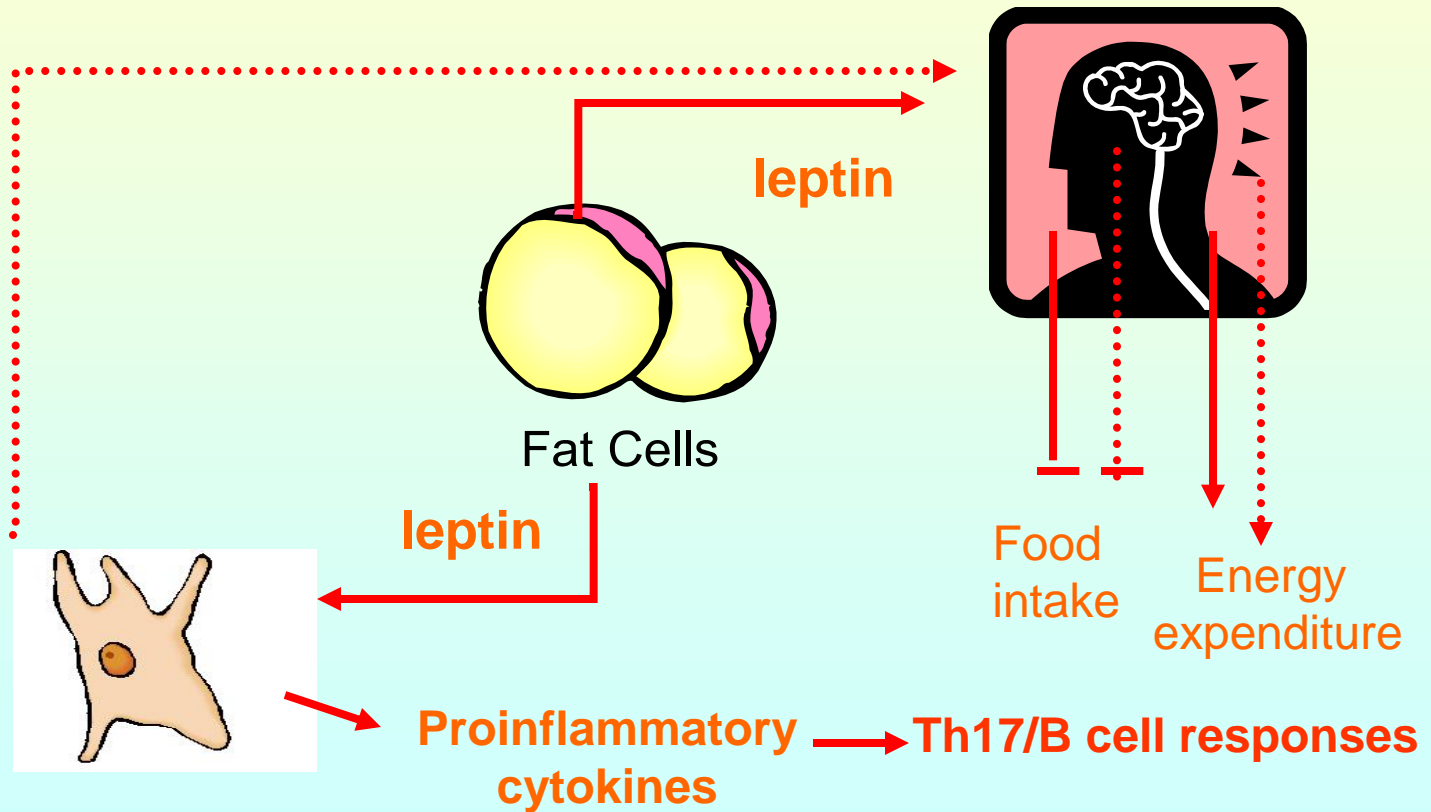


ObR:Fc IgG1



(Manuscript in preparation)

Roles of leptin in autoimmune response



Acknowledgements

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Xiang Lin
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