Platelet CD40L does not affect atherogenosis, but is a key player in atherothrombosis

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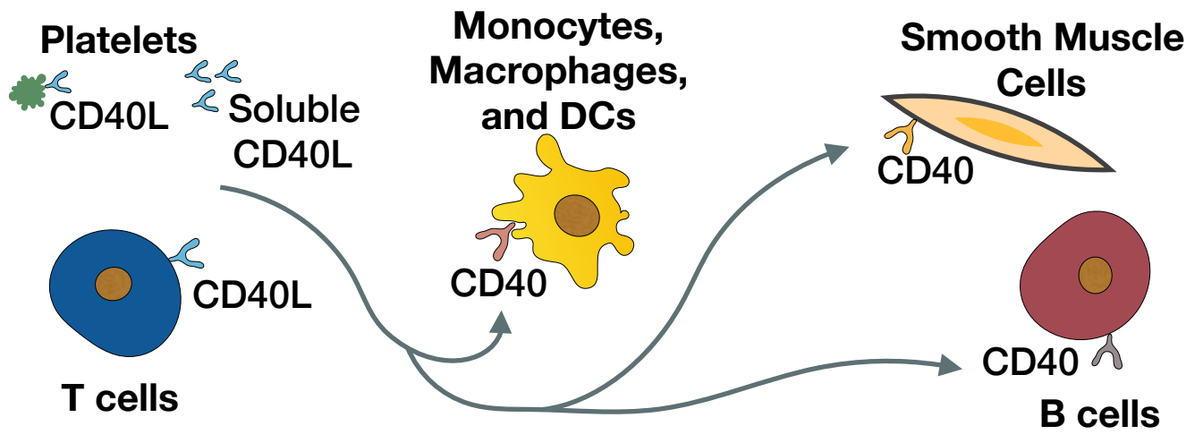
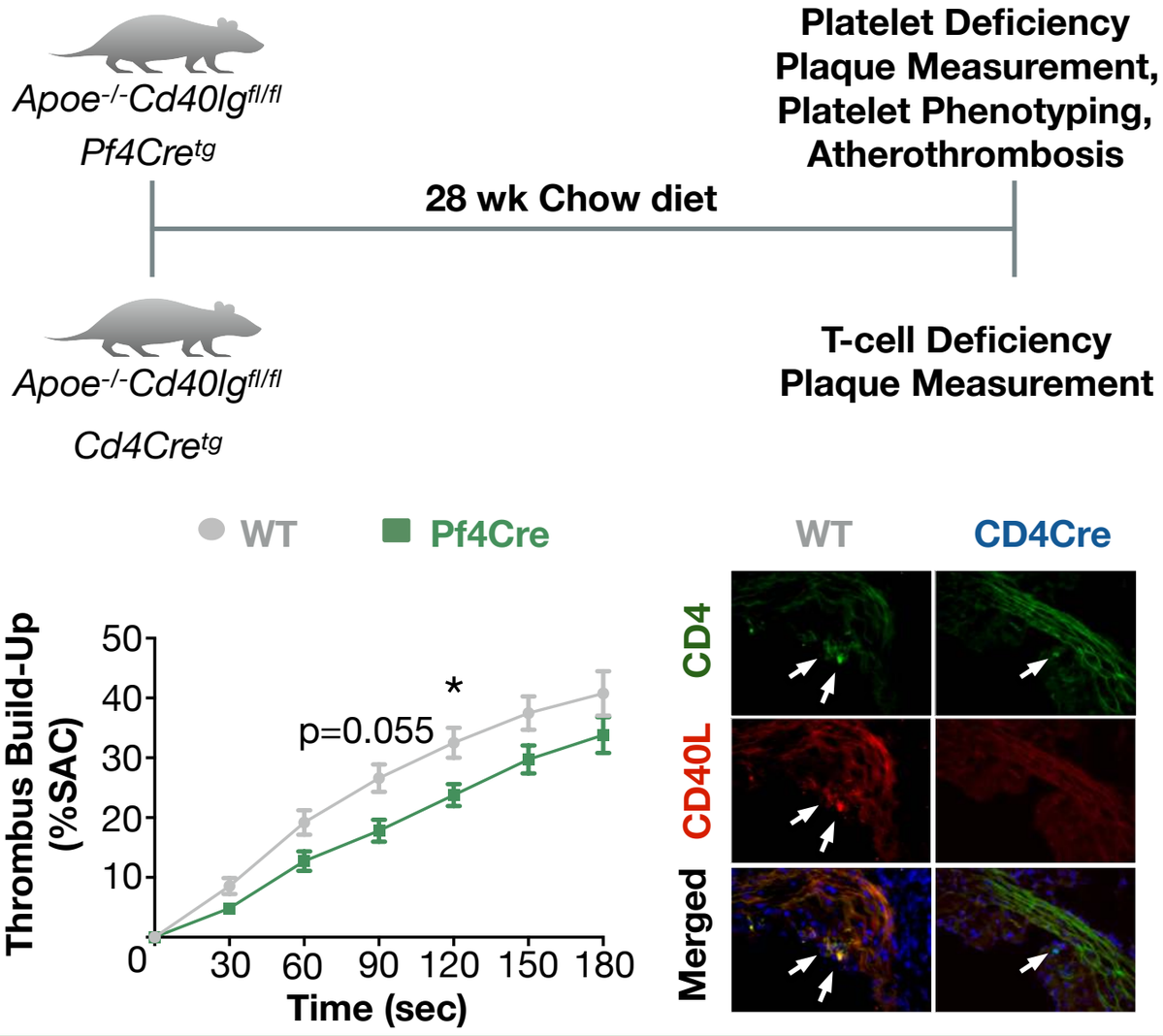
BACKGROUND

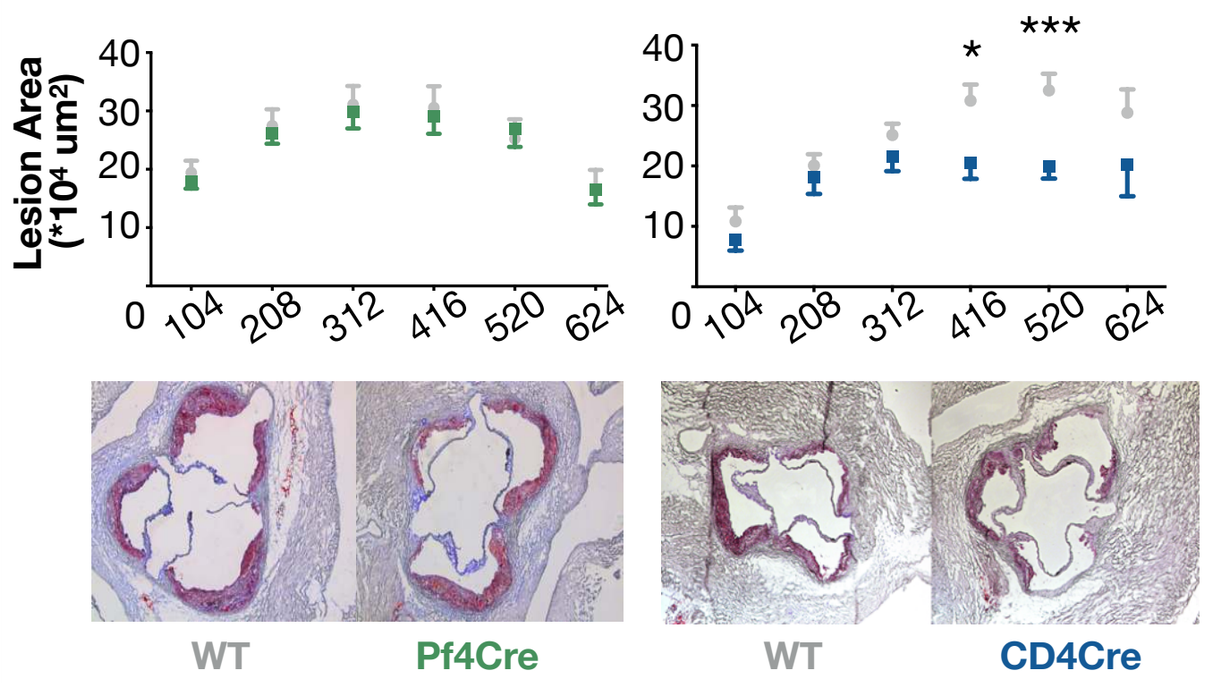
- The co-stimulatory **CD40-CD40L axis** is a major driver of atherosclerosis.
- Both **platelets** and **T cells** express express CD40L, but its **cell-specific role** and impact on **atherosclerosis** remains **elusive**.



EXPERIMENTAL PLAN

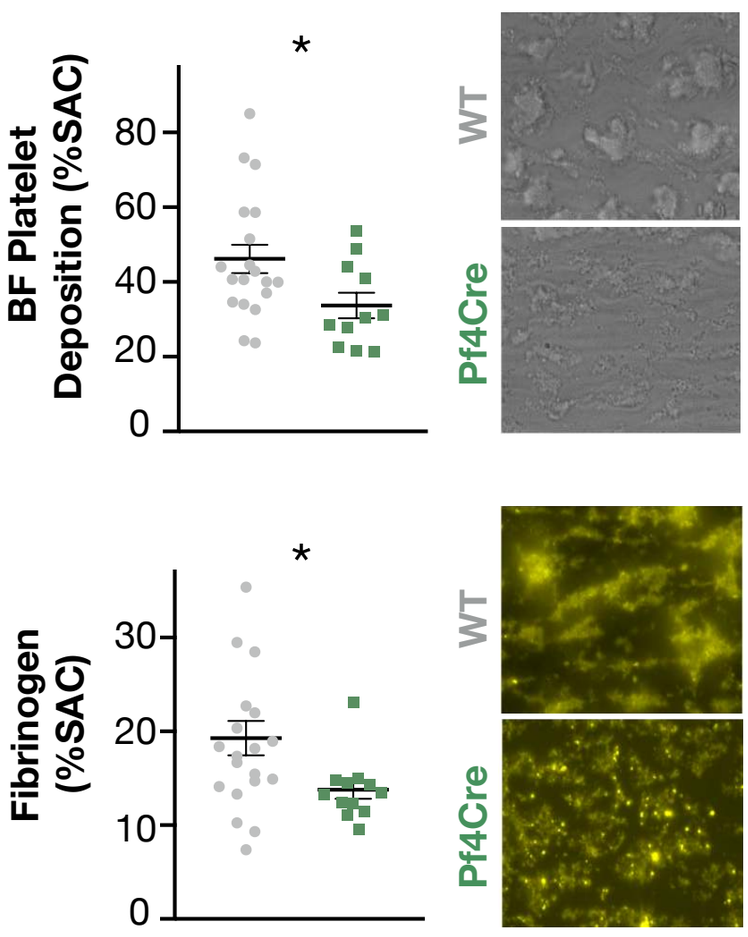


CELL-SPECIFIC DIFFERENCES IN PLAQUE BURDEN



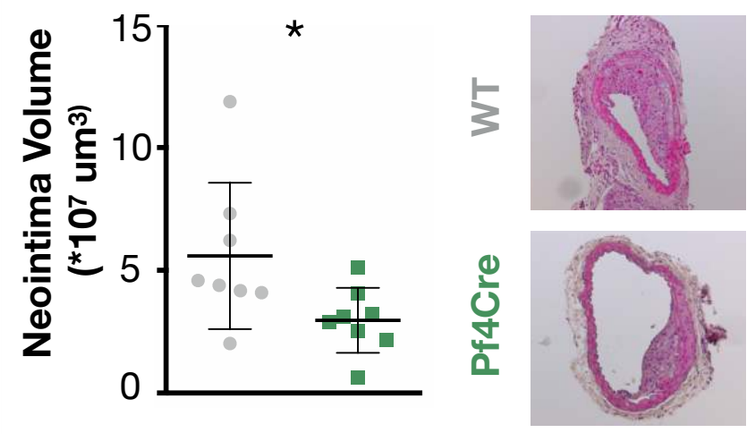
- **Oil-red O analysis** of aortic root plaques revealed a stark **difference in atherosclerotic** potential between **platelet** CD40L (left), where deficiency did not reduce plaque burden, versus **T-cell** CD40L (right), where deficiency attenuated atherosclerosis.

PHENOTYPING CD40L-DEFICIENT PLATELETS



- Considering its role in **thrombosis**, we continued to **phenotype** CD40L-deficient **platelets** via whole blood micro-spot perfusions.
- We observed **decreases** in **platelet deposition** (top) as well as **fibrinogen content** (bottom) in CD40L-deficient platelets.

PLATELET CD40L IN ATHEROTHROMBOSIS



- After phenotyping the platelets, we discovered a significant **reduction** in neointima volume following **wire injury**.

CONCLUSIONS

- Our data demonstrate **differing roles** for **platelet** and **T-cell CD40L** in atherosclerosis.
- Specifically, T-cell CD40L **mediates atherogenesis** while platelet CD40L plays **crucial roles** in **thrombus formation** as well as **neointima growth** following injury suggesting platelet CD40L plays a **key role** in **atherothrombosis**.

LEGEND

Apoe$^{-/-}$*Cd40lg*$^{fl/fl}$ — *Apoe*$^{-/-}$*Cd40lg*$^{fl/fl}$ *Pf4Cre*^{tg} — *Apoe*$^{-/-}$*Cd40lg*$^{fl/fl}$ *Cd4Cre*^{tg}

P values: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$