Immunity

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Dietary Fiber Confers Protection against Flu by Shaping Ly6c⁻ Patrolling Monocyte Hematopoiesis and CD8⁺ T Cell Metabolism

Aurélien Trompette,[1,5] Eva S. Gollwitzer,[1,3,5] Céline Pattaroni,[1,4] Isabel C. Lopez-Mejia,[2] Erika Riva,[1] Julie Pernot,[1] Niki Ubags,[1] Lluis Fajas,[2] Laurent P. Nicod,[1] and Benjamin J. Marsland[1,4,6,*]

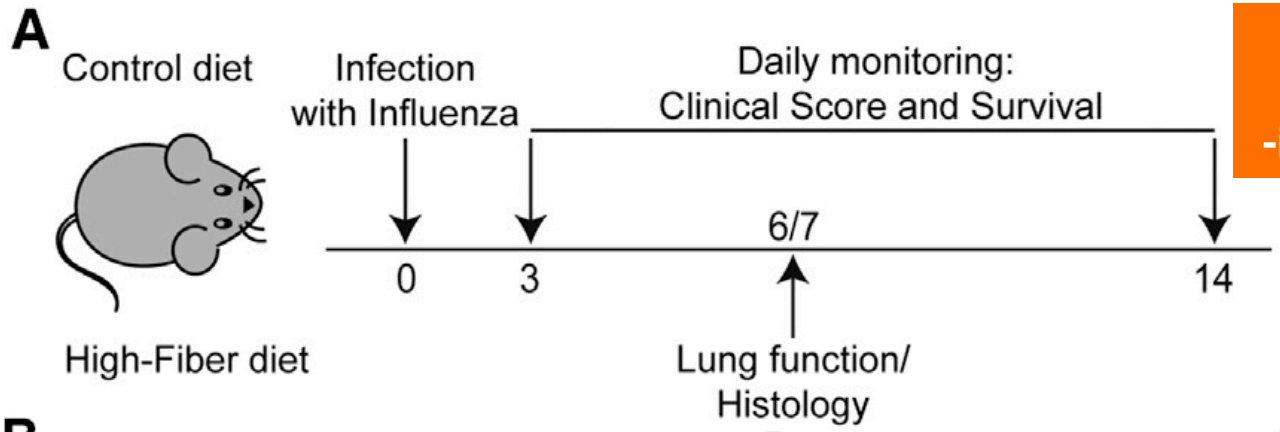
Background: Dietary fiber improves intestinal health and protects against chronic inflammatory diseases by dampening immune responses through SCFAs.

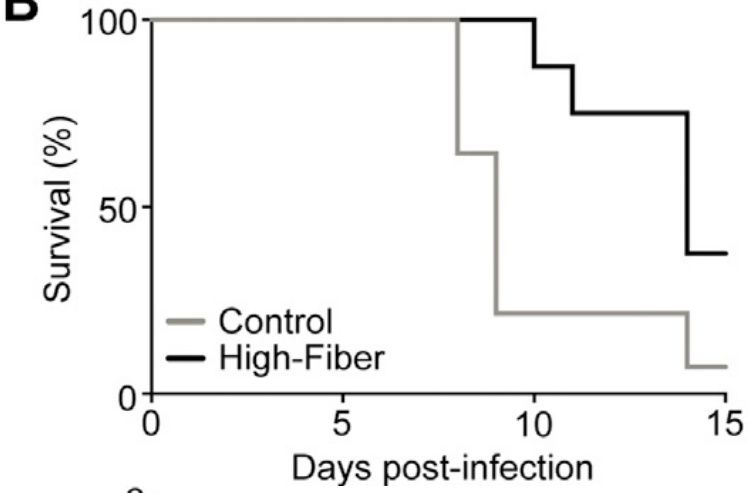
Motivation: To address whether fermentable dietary fiber influences antiviral immunity, where the anti-inflammatory property of SCFAs in principle could prevent protective immunity.

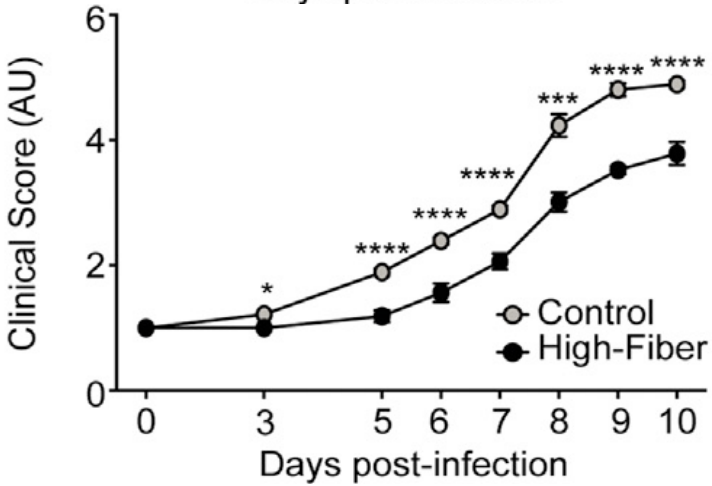
Experiments: High-dose influenza A infection feed with control (cellulose) versus high-fiber diet (inulin), and assessed influenza-induced immunopathology, gut microbiome composition, bone marrow hematopoeisis, CD8+ T cells metabolism.

Results:
a) Dietary fiber protects against influenza induced pathology by altering gut microbial composition and SCFA levels.
b) Dietary fiber alters bone marrow hematopoiesis and boosts Ly6c⁻ patrolling monocytes, leading to blunted chemokine CXCL1 production in airways and reduced neutrophil-mediated tissue damage.
c) Dietary fiber increases antiviral immunity through activating CD8+ T cells and altering their metabolism.

Fig. 1 Inulin protects against influenza -induced immunopathology







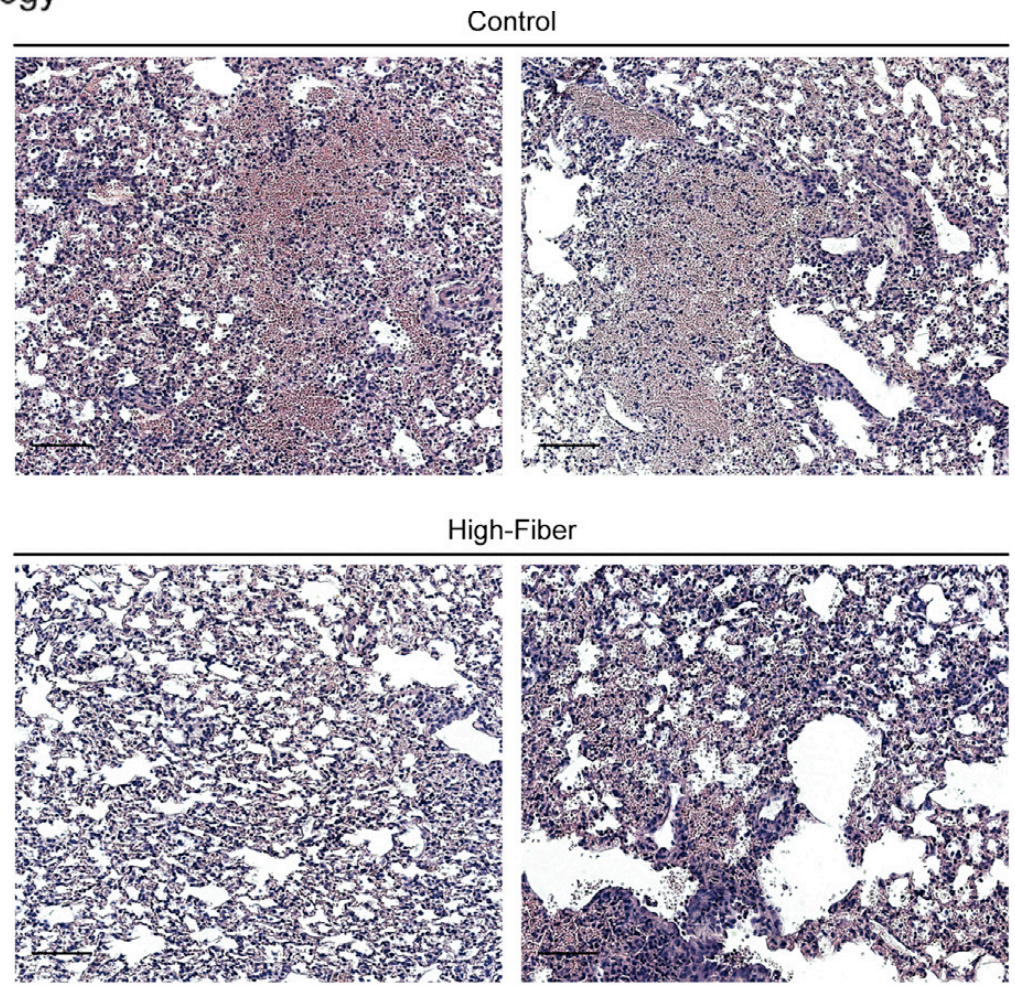
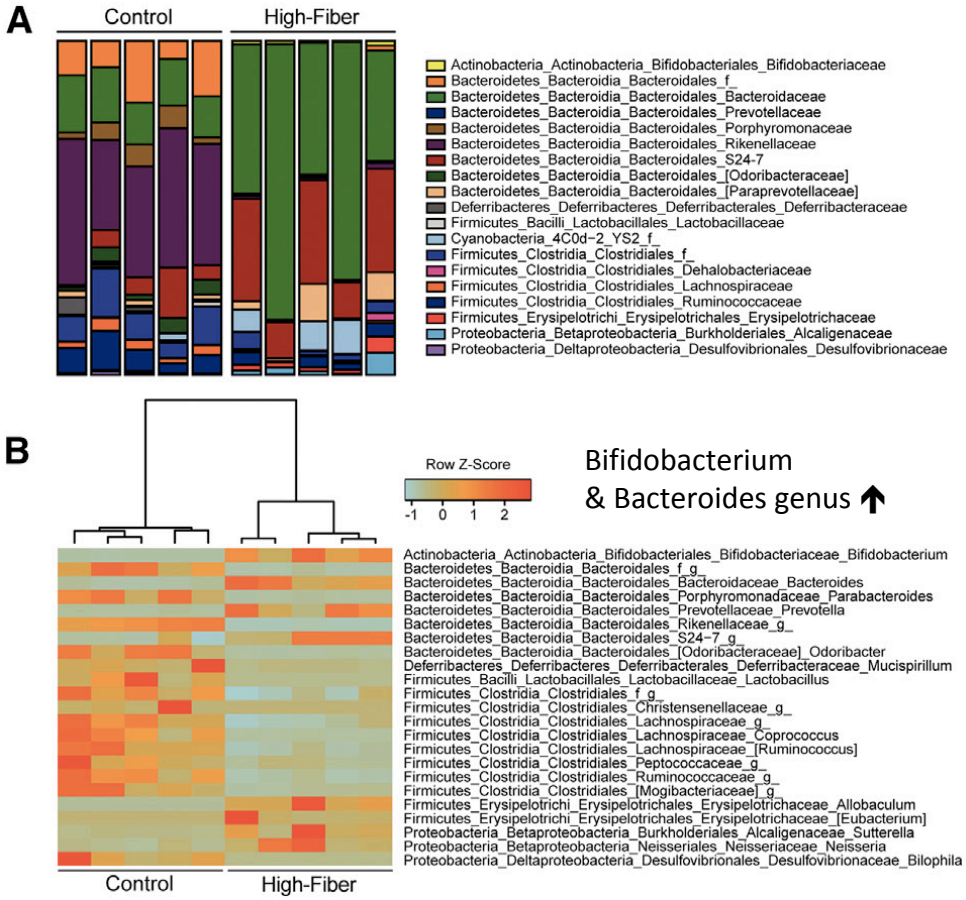
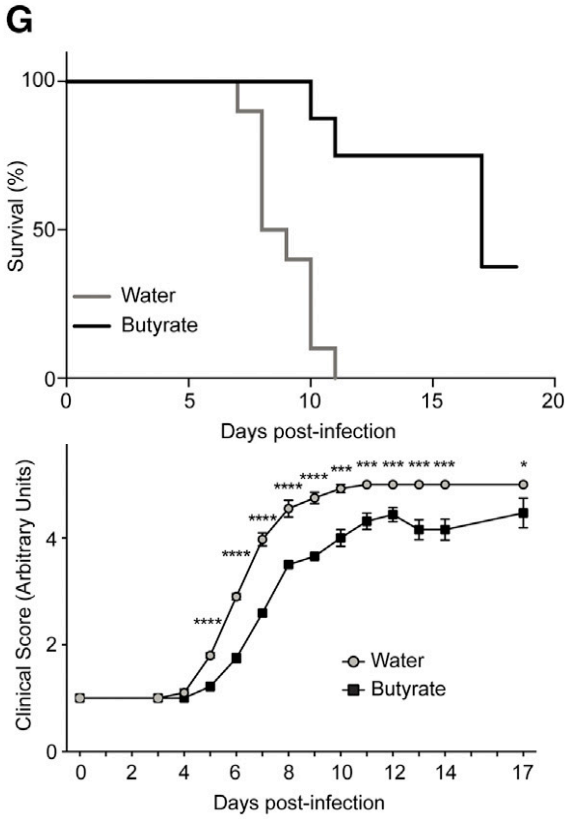
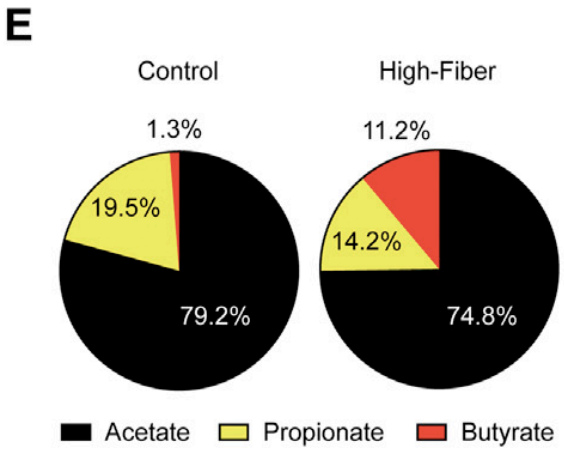
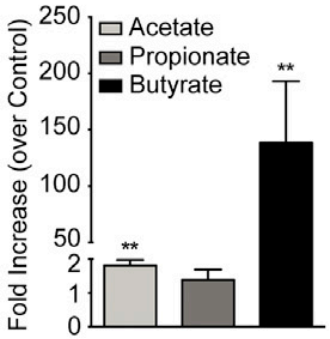


Fig. 2 Inulin alters gut microbiota and exhibits butyrogenic properties









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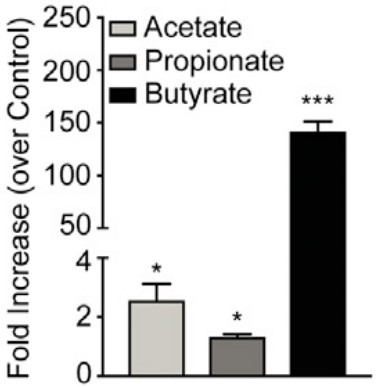
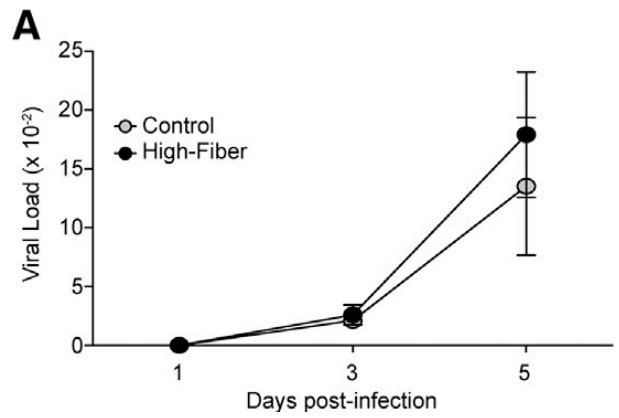
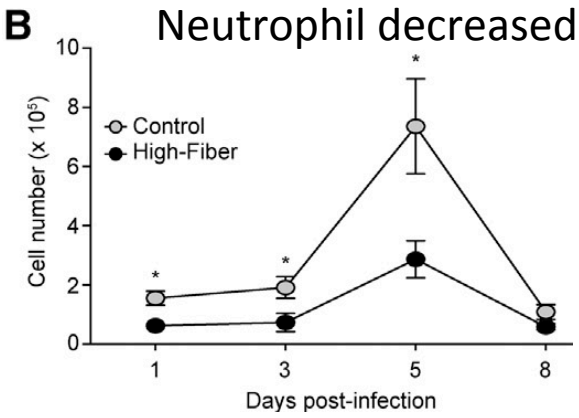
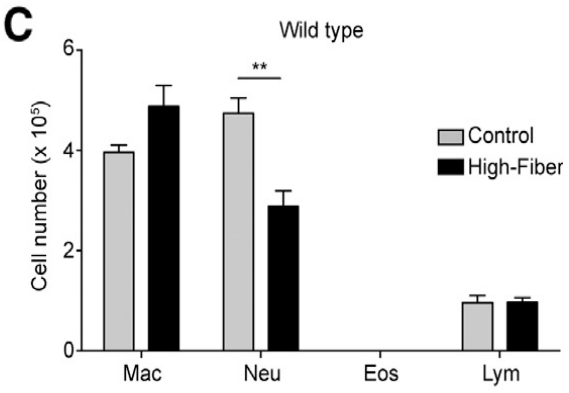


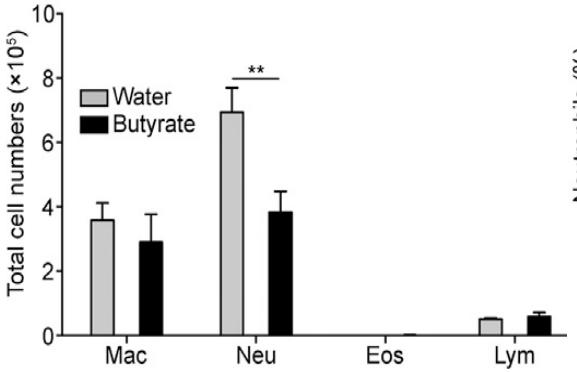
Neutrophil decreased

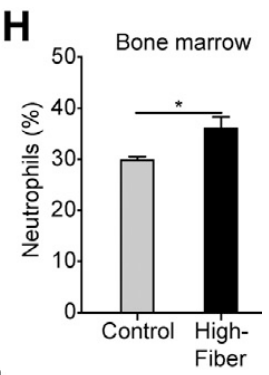
Fig. 3 Dietary fiber prevents excessive neutrophil influx into airways by reducing macrophage-derived CXCL1 production

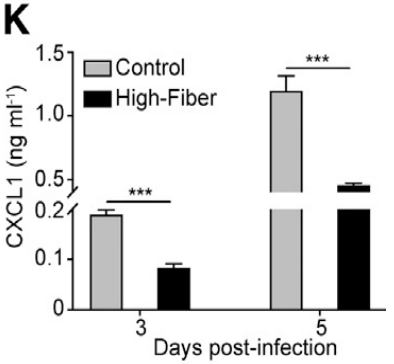






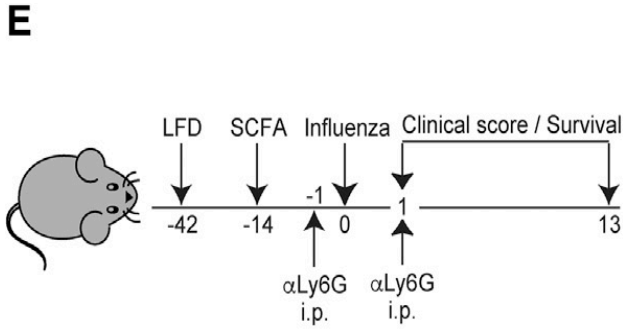


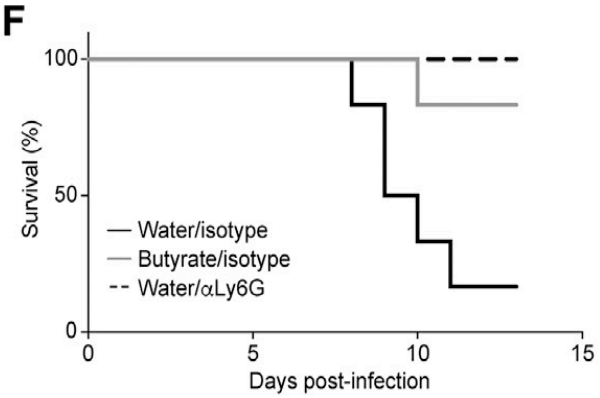




CXCL1 is a neutrophil chemoattractant

Neutrophil decreased responsible for increased survival?





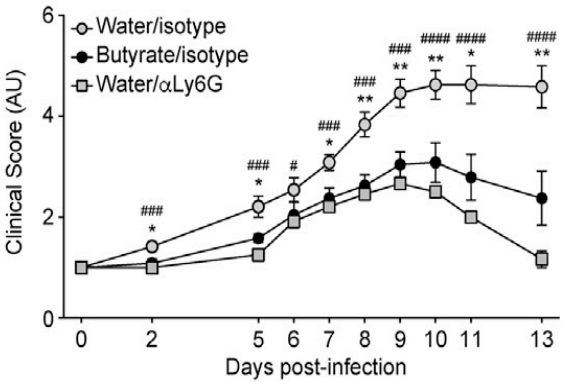
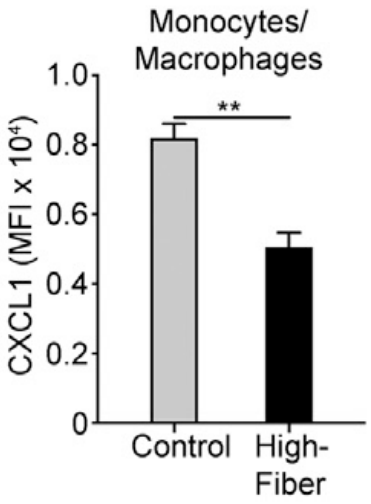
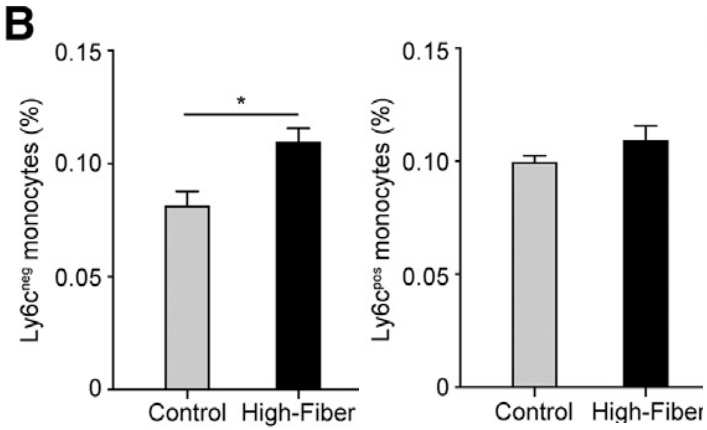
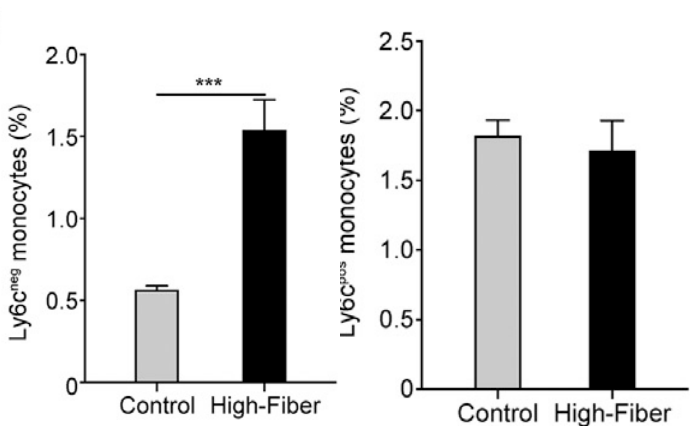


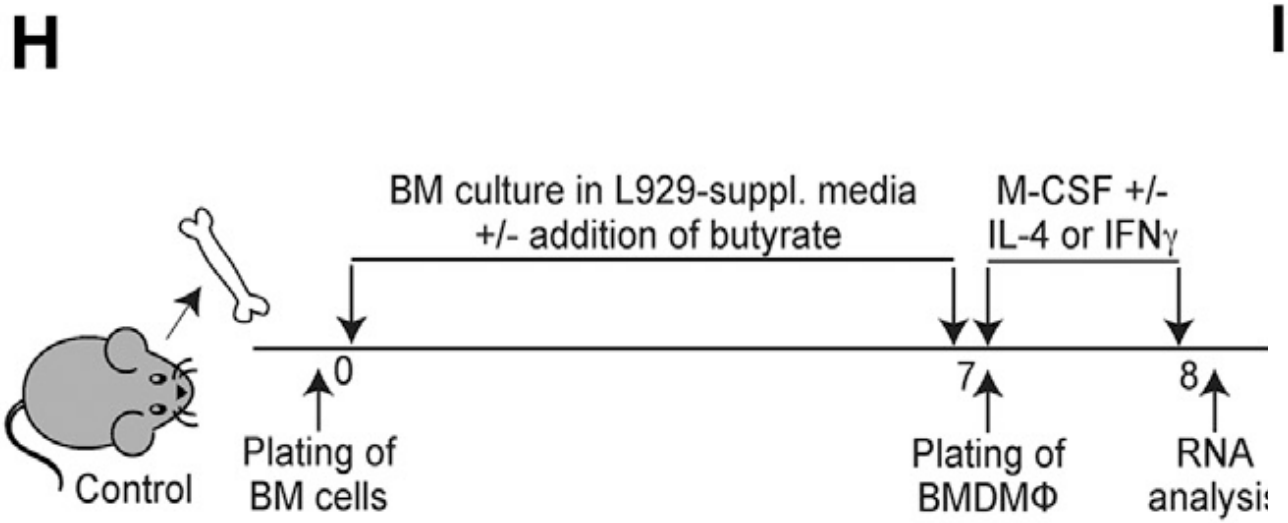
Fig. 4 Dietary fiber enhances bone marrow hematopoeisis of Ly6c^{--} patrolling monocytes

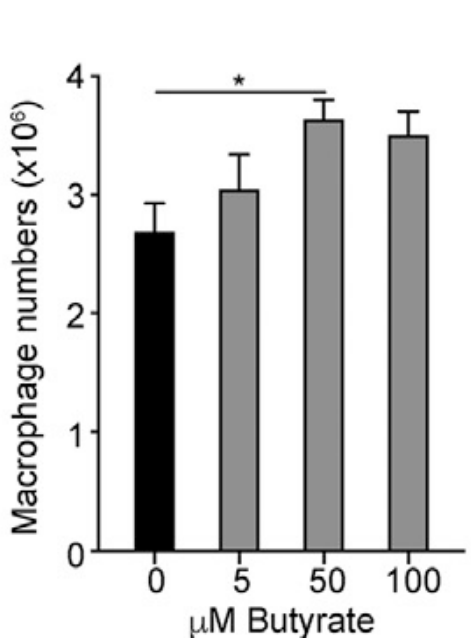






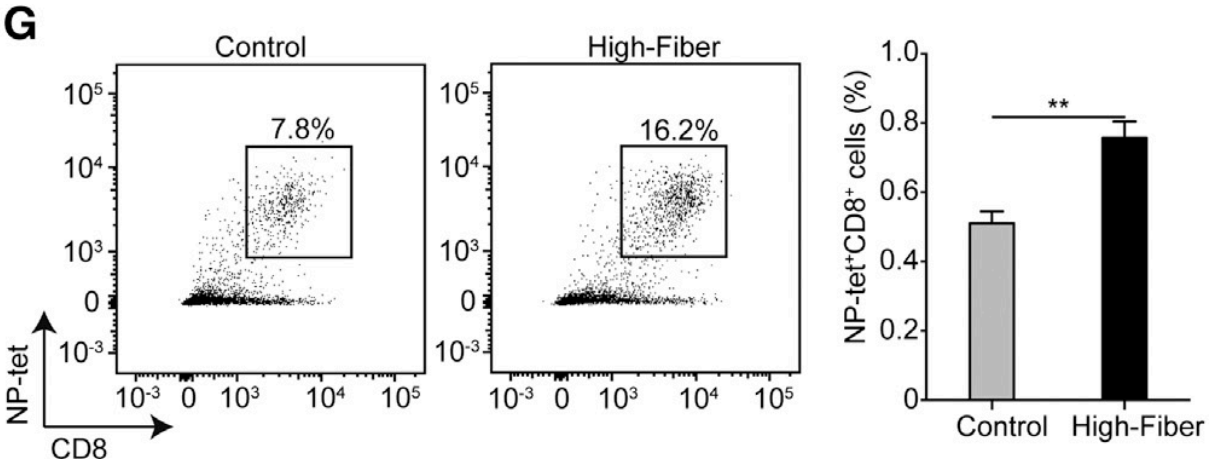
Ly6c+ inflammatory monocytes: no change
Ly6c- cells increased (in bone marrow and lung)

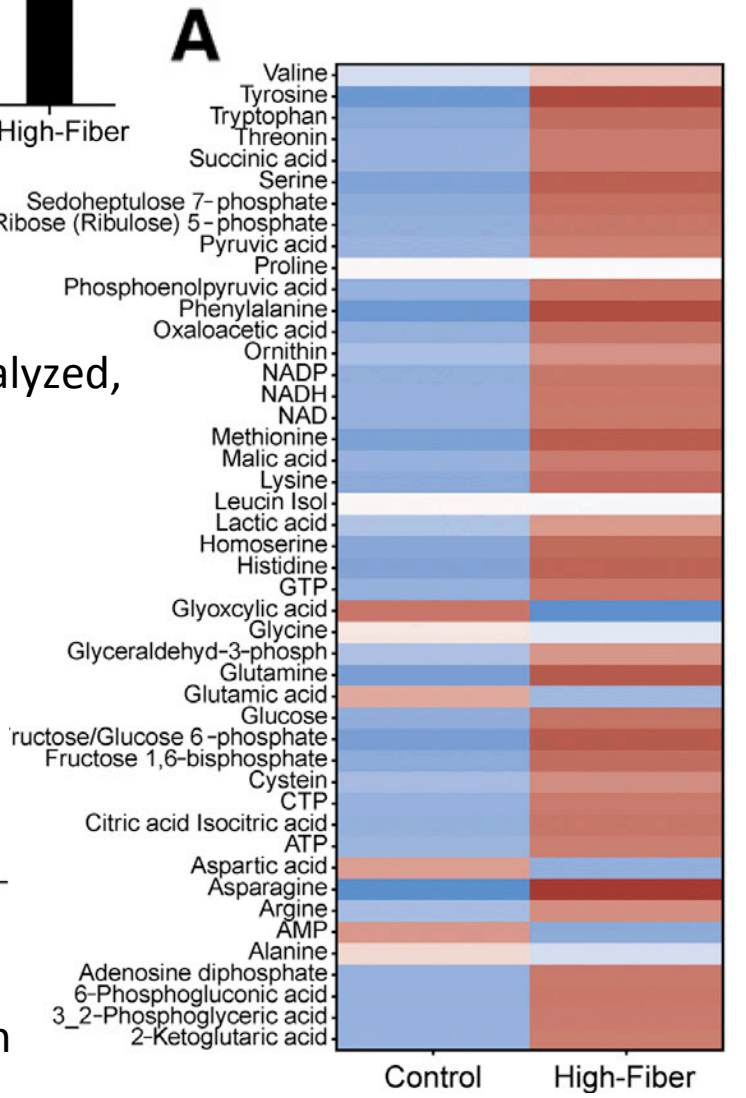




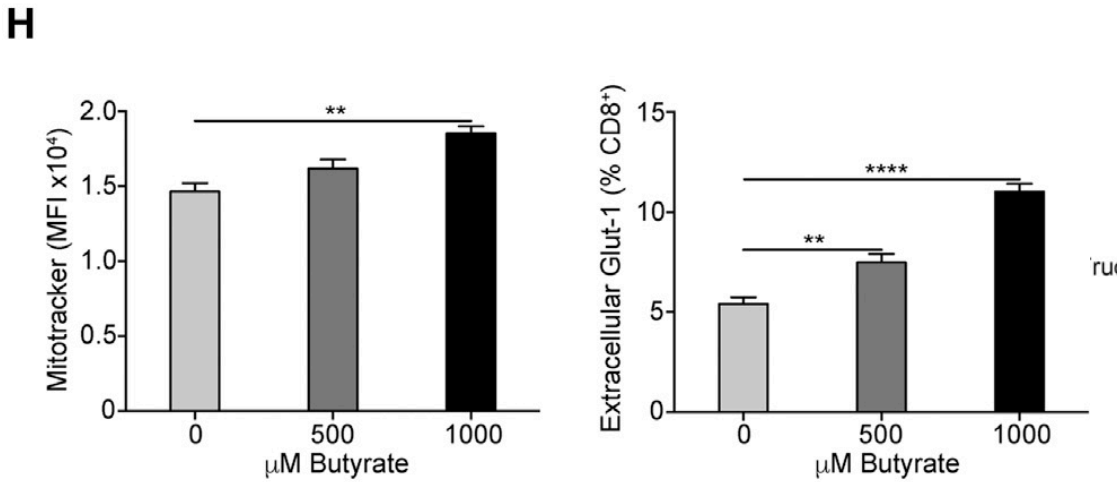
Ex vivo differentiation from bone marrow cells to macrophages

Fig. 5&6 Dietary fiber boosts antiviral CD8+ T cell response and influences its metabolism



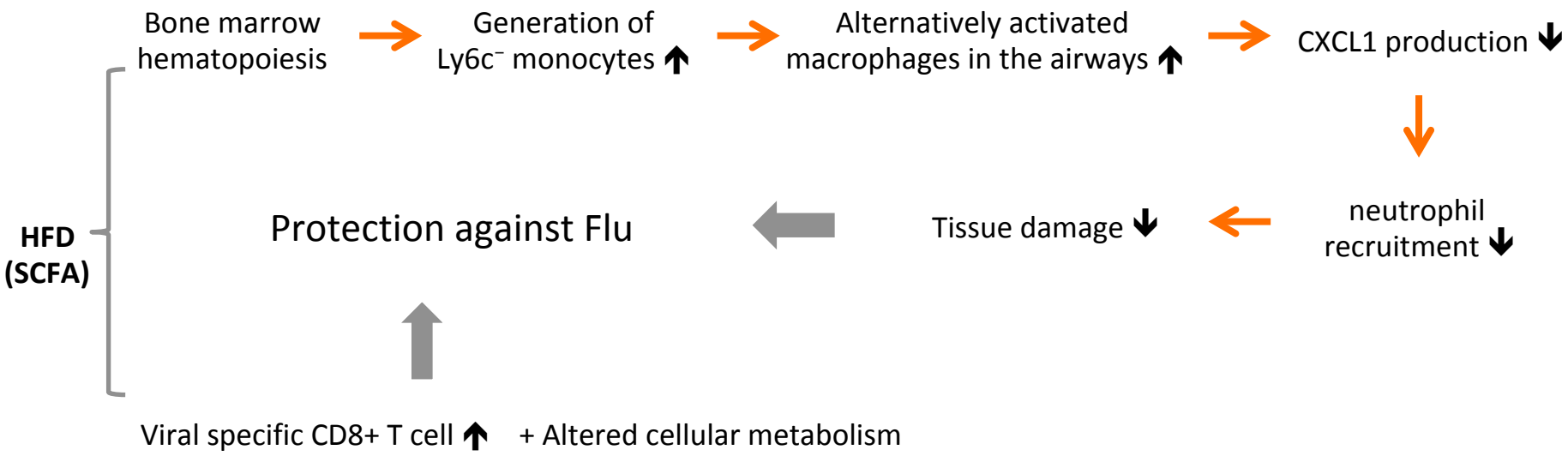


"Navie CD8+ T cells from HFD-fed mice exhibited elevated concentrations of most of metabolites analyzed, notably those of tricarboxylic acid cycle."



Increased mitochondrial mass and surface Glut-1 expression with butyrate stimulation

Summary


Bone marrow hematopoiesis
Generation of Ly6c⁻ monocytes ↑
Alternatively activated macrophages in the airways ↑
CXCL1 production ↓
neutrophil recruitment ↓
Tissue damage ↓
Protection against Flu
HFD (SCFA)
Viral specific CD8+ T cell ↑
+ Altered cellular metabolism