

A Multi-Omics Approach Demonstrates that Spaceflight Leads to Lipid Accumulation in Mouse Livers

National Aeronautics and
Space Administration



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FEMALE ASTRONAUT



Women suffer less from hearing loss with advancing age, and do not display a bias towards loss of hearing in the left ear



Women demonstrate a slight bias towards accuracy versus speed in response to an alertness test



Women mount more potent immune responses



Struvite kidney stones more common in women



Female astronauts, (to date) do not exhibit clinically significant visual impairment



Large individual variability to muscle and bone loss in women



Health effect observed on Earth

MALE ASTRONAUT



Men suffer more from hearing loss with advancing age, and display a bias towards loss of hearing in the left ear



Men mount less potent immune responses



Calcium oxalate kidney stones more common in men



Some male astronauts exhibit clinically significant visual impairment

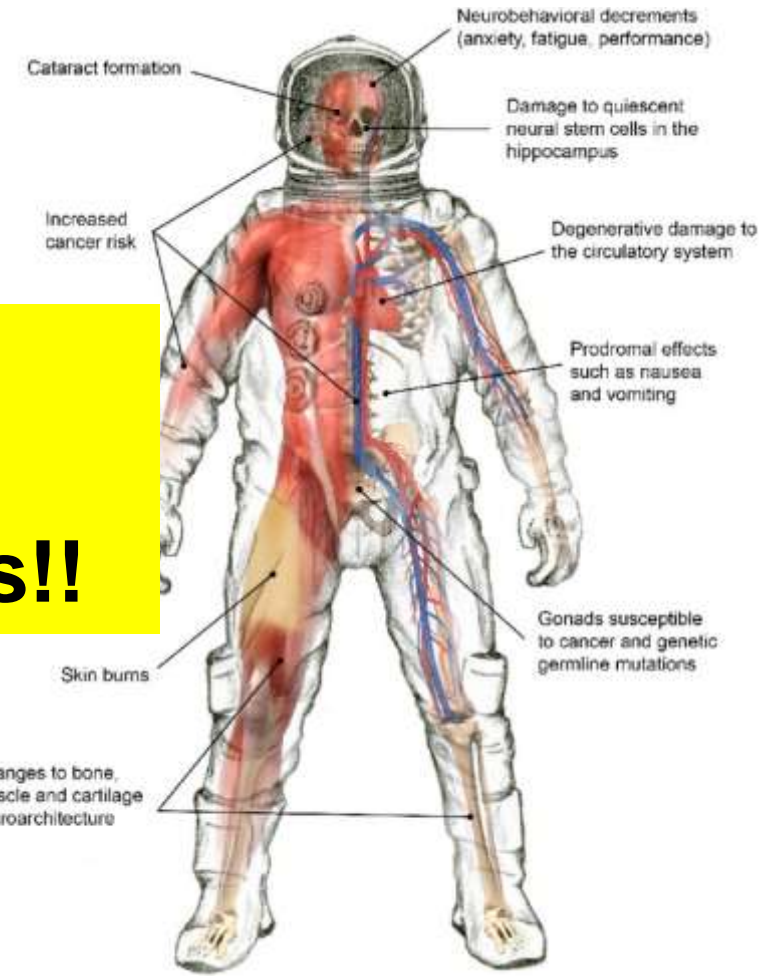


Large individual variability to muscle and bone loss in men



Health effect observed in space

One thing is always missing: LIVER as organ of interest for spaceflight related health risks!!



Select health effects due to space radiation exposures.

From: J. Chancellor et al., Space Radiation: The Number One Risk to Astronaut Health beyond Low Earth Orbit. *Life*, 4(3), 491-510;



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Keywords



Welcome to NASA GeneLab - the first comprehensive space-related omics database; users can upload, download, share, store, and analyze spaceflight and spaceflight-relevant data from experiments using model organisms.



Data Repository

Search and upload spaceflight datasets



Analyze Data

Perform large-scale analysis of biological omics data



Environmental Data

Radiation data collected during experiments conducted in space



Collaborative Workspace

Share, organize and store files



Submit Data

Have space-relevant data to submit to GeneLab?



Tutorials

New to GeneLab?

LATEST DATA RELEASES

TRANSCRIPTOMICS



NEW! GLDS-255: Spaceflight influences gene expression, photoreceptor integrity, and oxidative stress-related damage in the murine retina

EPIGENOMICS / METAGENOMICS

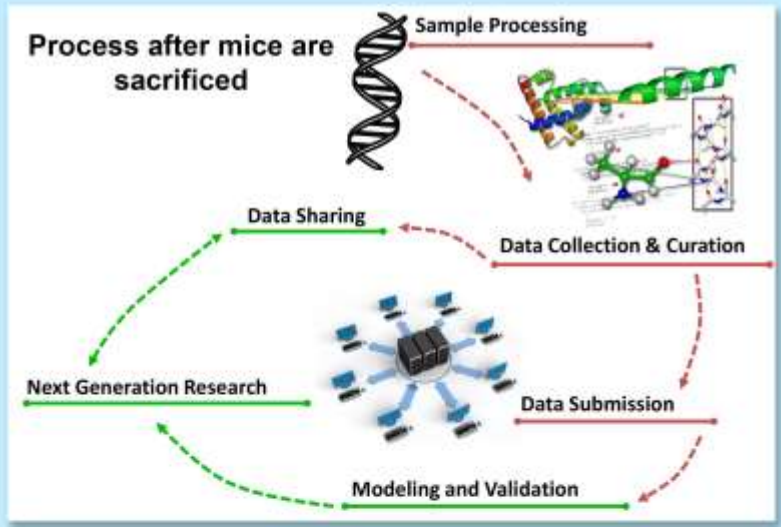


NEW! GLDS-250: Metagenomic analysis of feces from mice flown on the RR-9 mission

PROTEOMICS / METABOLOMICS

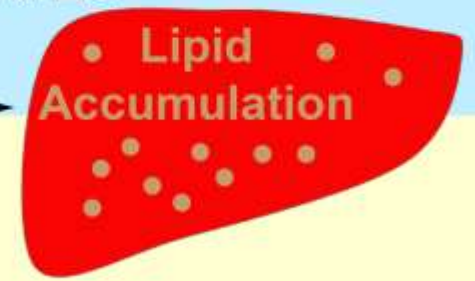
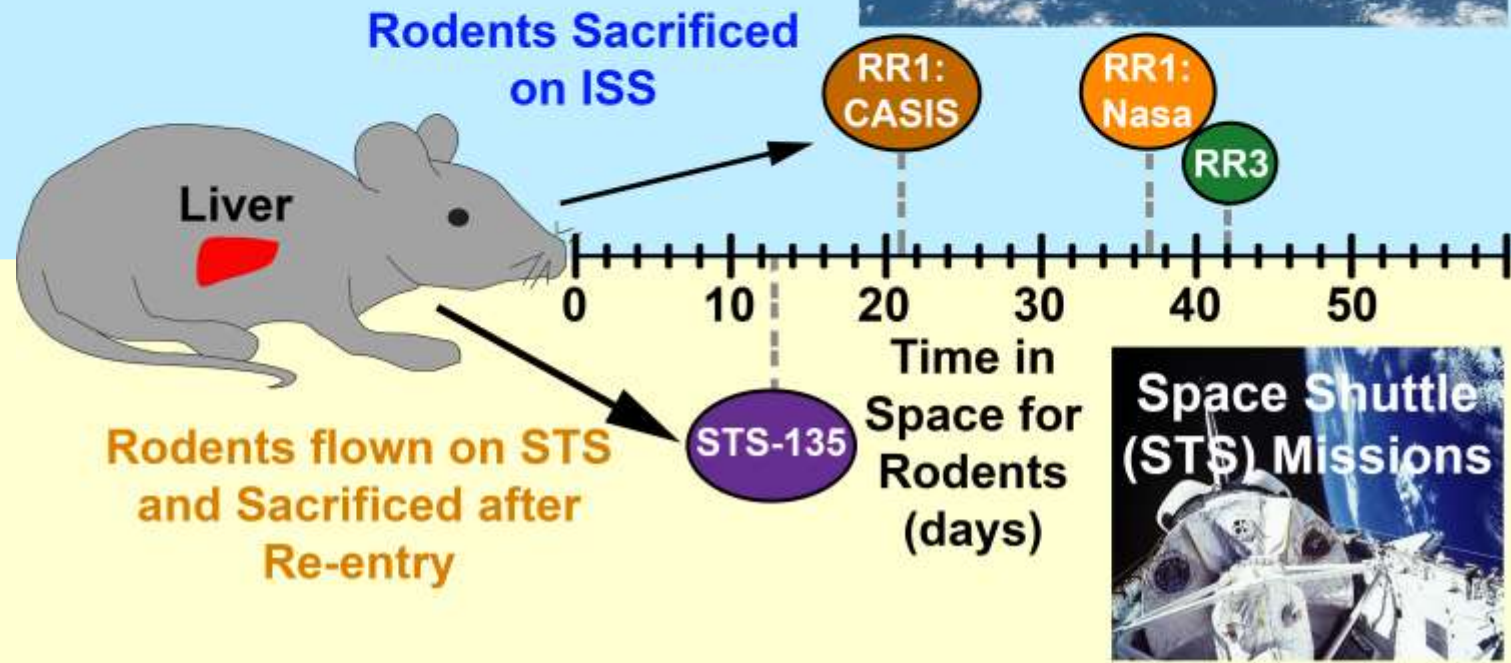


GLDS-209: Re-Adaption on Earth after Spaceflights Affects the Mouse Liver Proteome



Liver after Spaceflight

- ↑ Lipid Metabolism
- ↑ Fatty Acid Metabolism
- ↑ NAFLD



RESEARCH ARTICLE

Spaceflight Activates Lipotoxic Pathways in

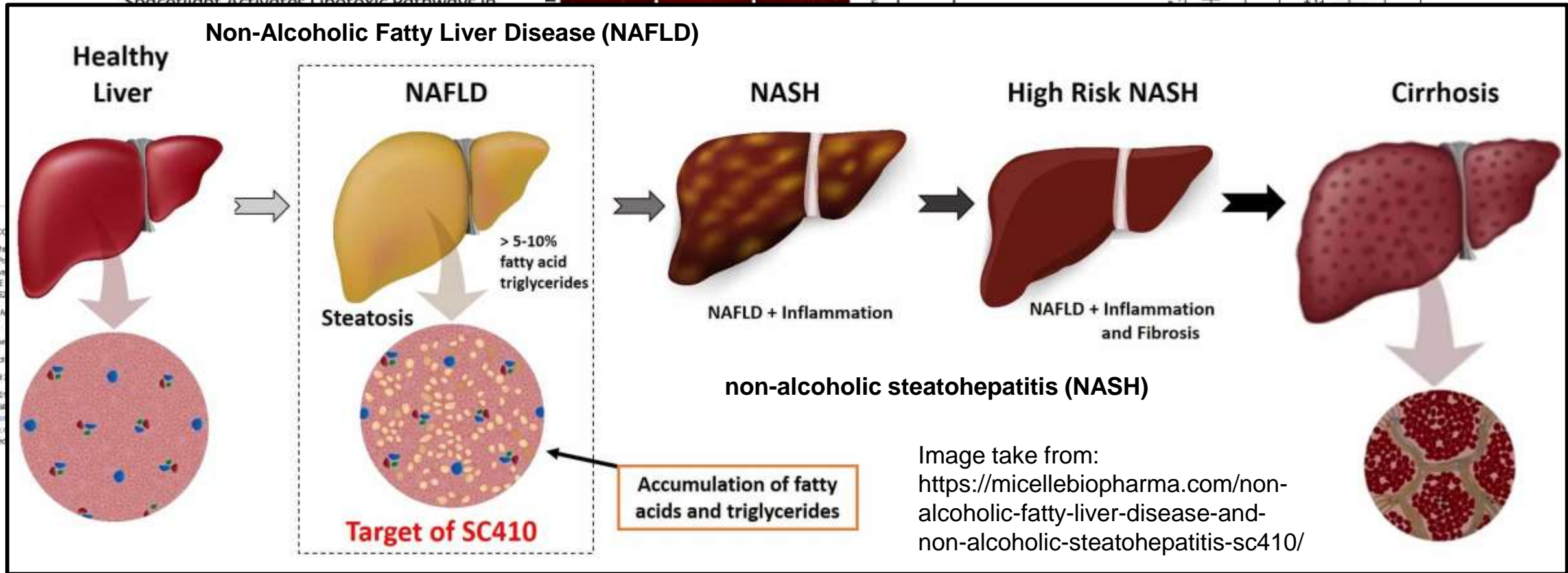
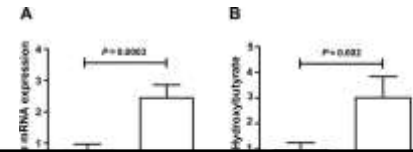
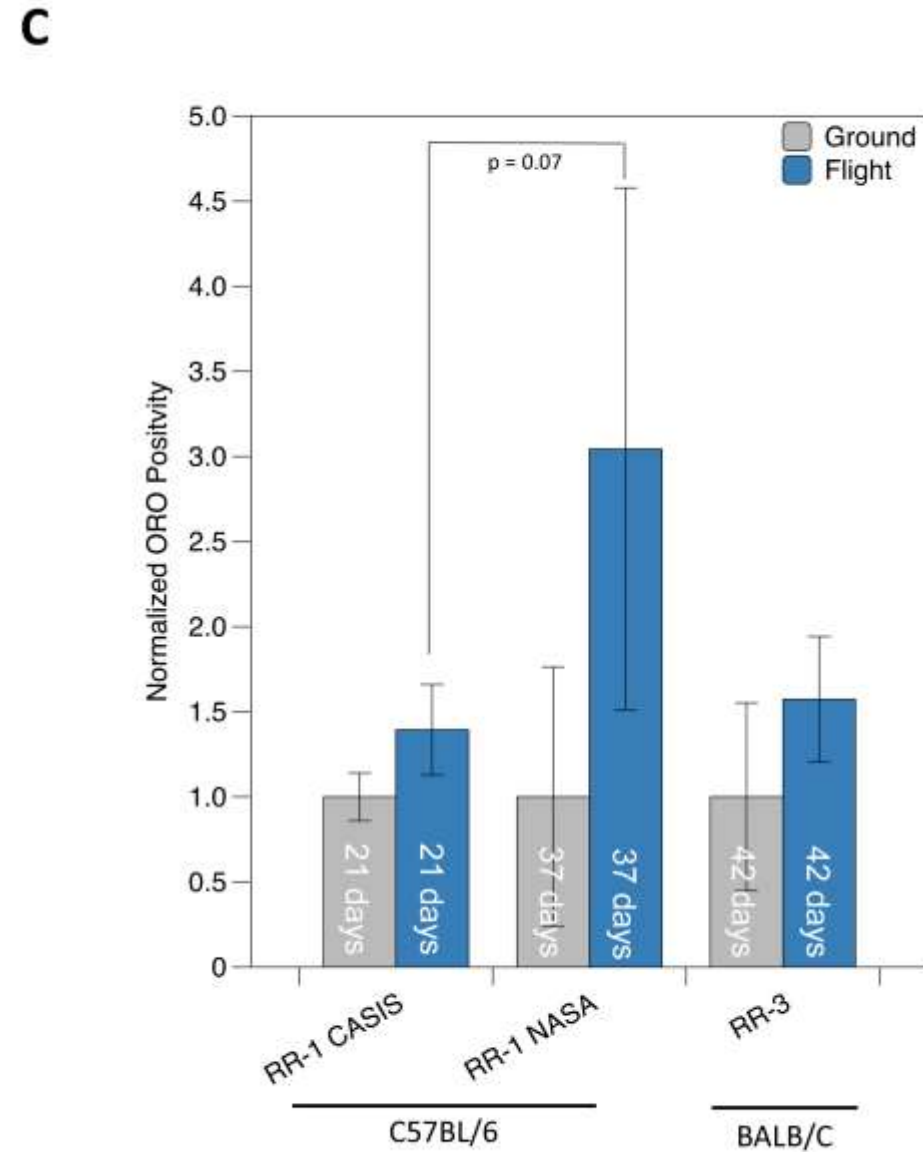
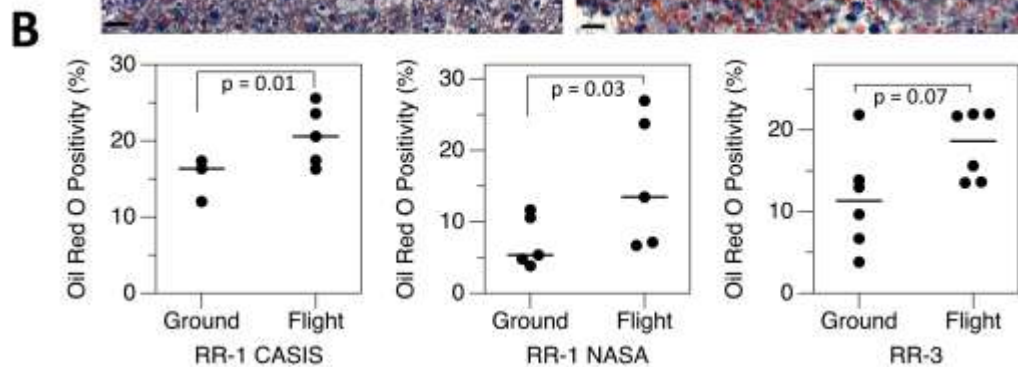
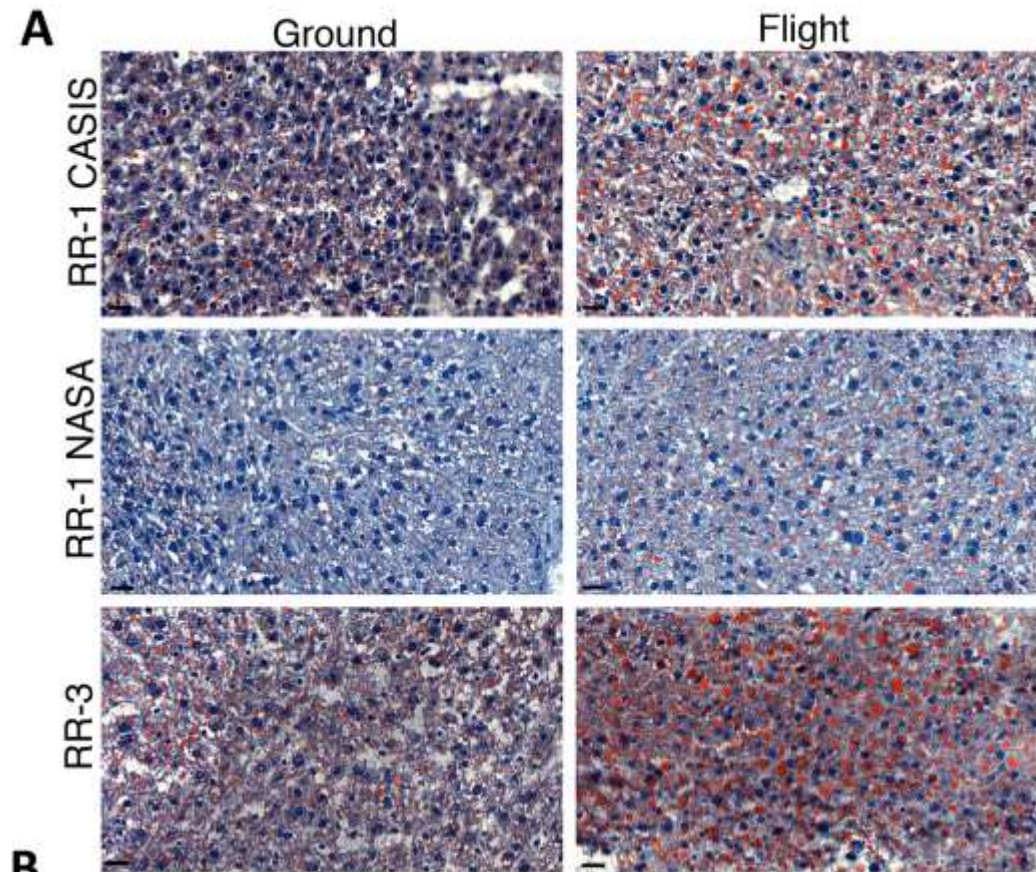


Fig 2. Spaceflight mice have increased accumulation of hepatic lipid droplets. A) Frozen liver tissue was cryosectioned using OCT solution and sections imaged by CARS at a magnification of 60x. Representative images are shown from 3 different animals in each group. Images from AEM ground controls appear on the top panel and FLT mice on the bottom panel. B) Multiple regions were imaged from 2 cryosections taken at different tissue depths per animal (n = 5/group). Images were processed using ImageJ.

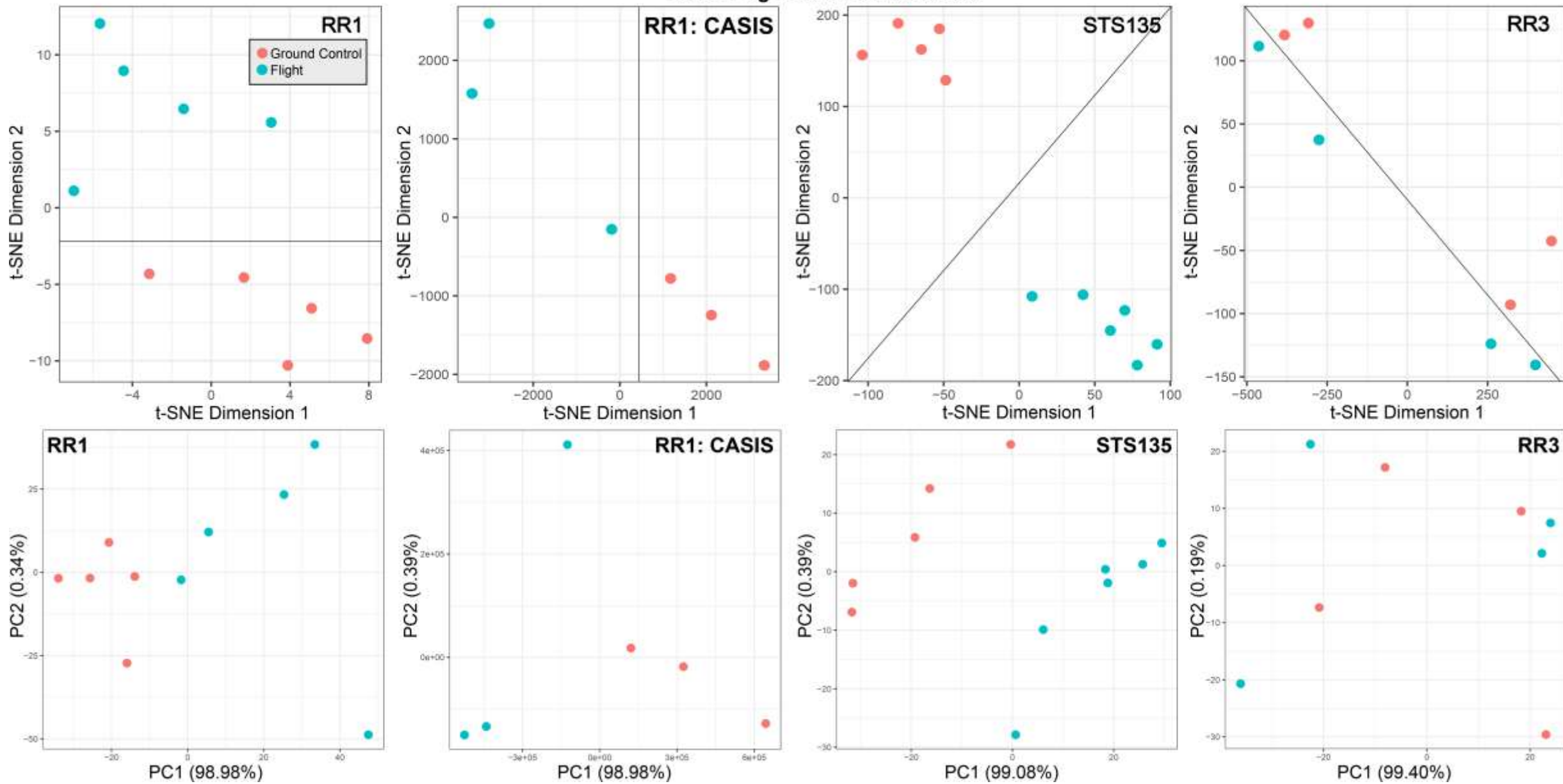
Fig 7. Spaceflight induces activation of PPARα pathways maintained by a feedback loop involving hepatic thioesterase activity and mediated by DHA. Elements of the space environment such as microgravity, oxidative stress and radiation may lead to activation of the PPARα-RXRα heterodimer by ω-3 fatty acids (including DHA), PGC-1α and retinoids from activated HSCs, increasing thioesterase activity. Hepatic steatosis, as well as synthesis of bile acids, ketone bodies and dicarboxylic acids, results from activation of downstream pathways. Fibrosis may also ensue from transformation of the activated HSCs. DHA and bile acids are ligands for FXR, which may be activated in a compensatory manner and help protect from HSC-induced remodeling of the ECM. PPRE, peroxisome proliferator response element.



Citation: Josech JL, Orlicky DJ, Po Spaceflight Activates Lipotoxic Pathways in Liver. PLOS ONE journal.pone.0195202
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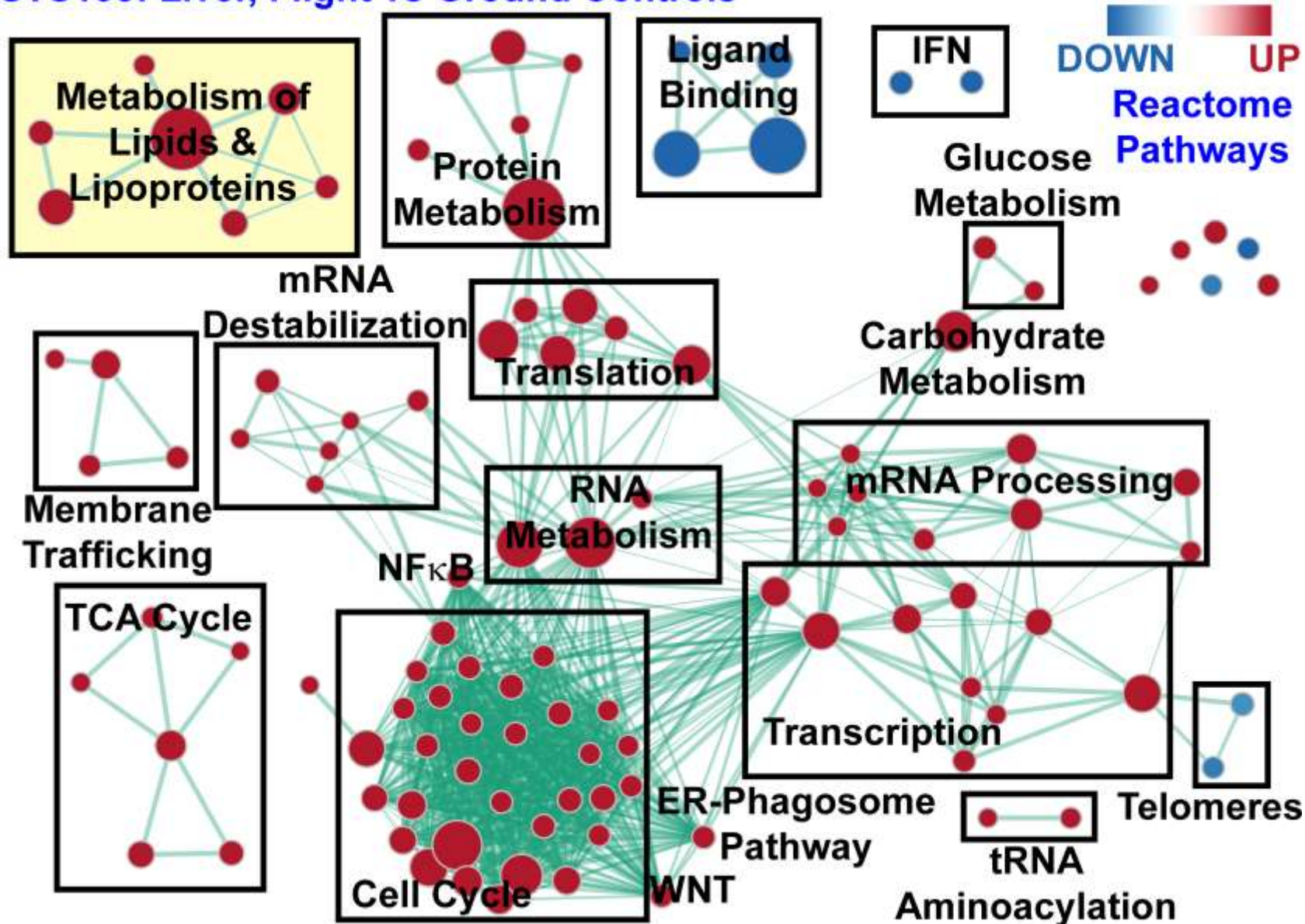


Liver: Flight vs Ground Control

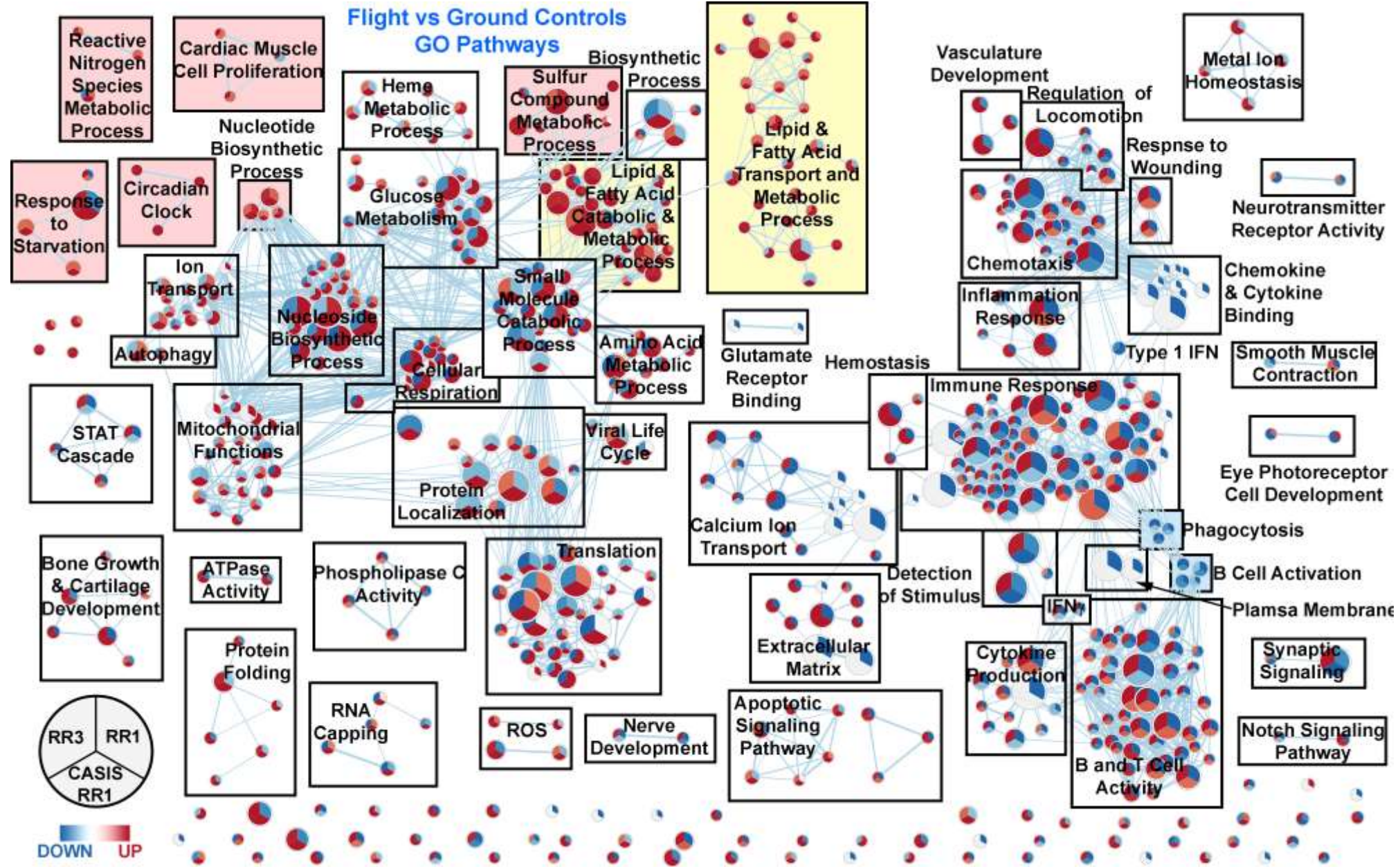


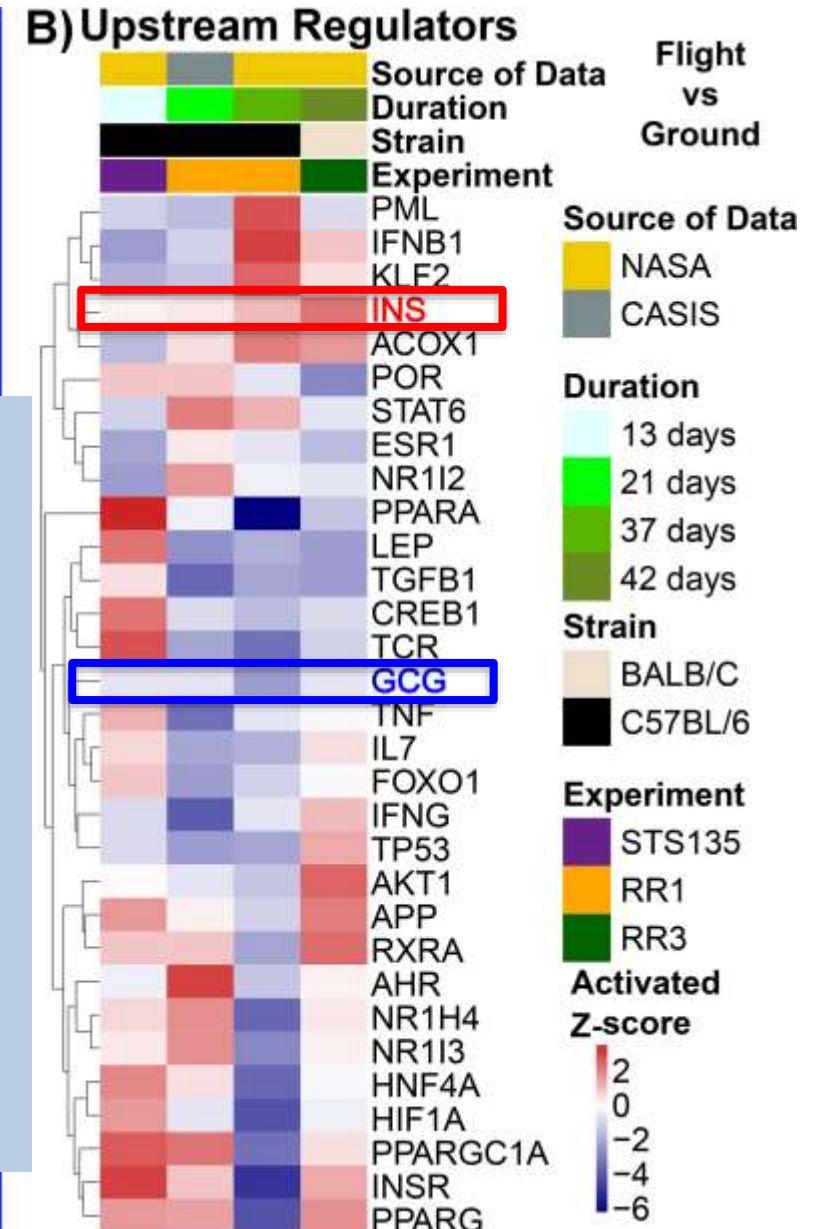
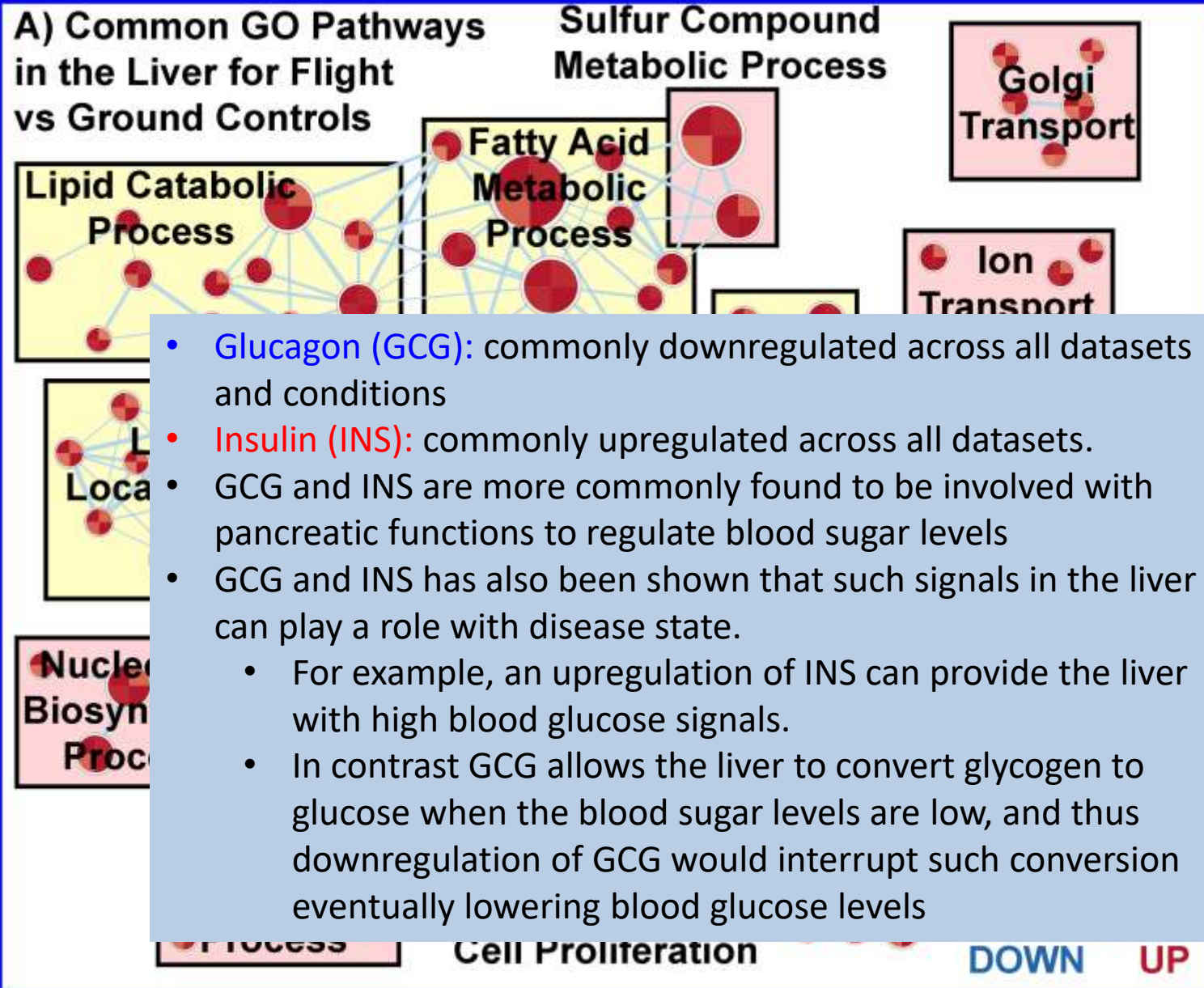
GSEA Analysis on STS-135 Liver Samples Reveals Dysregulation with Lipid Related Pathways

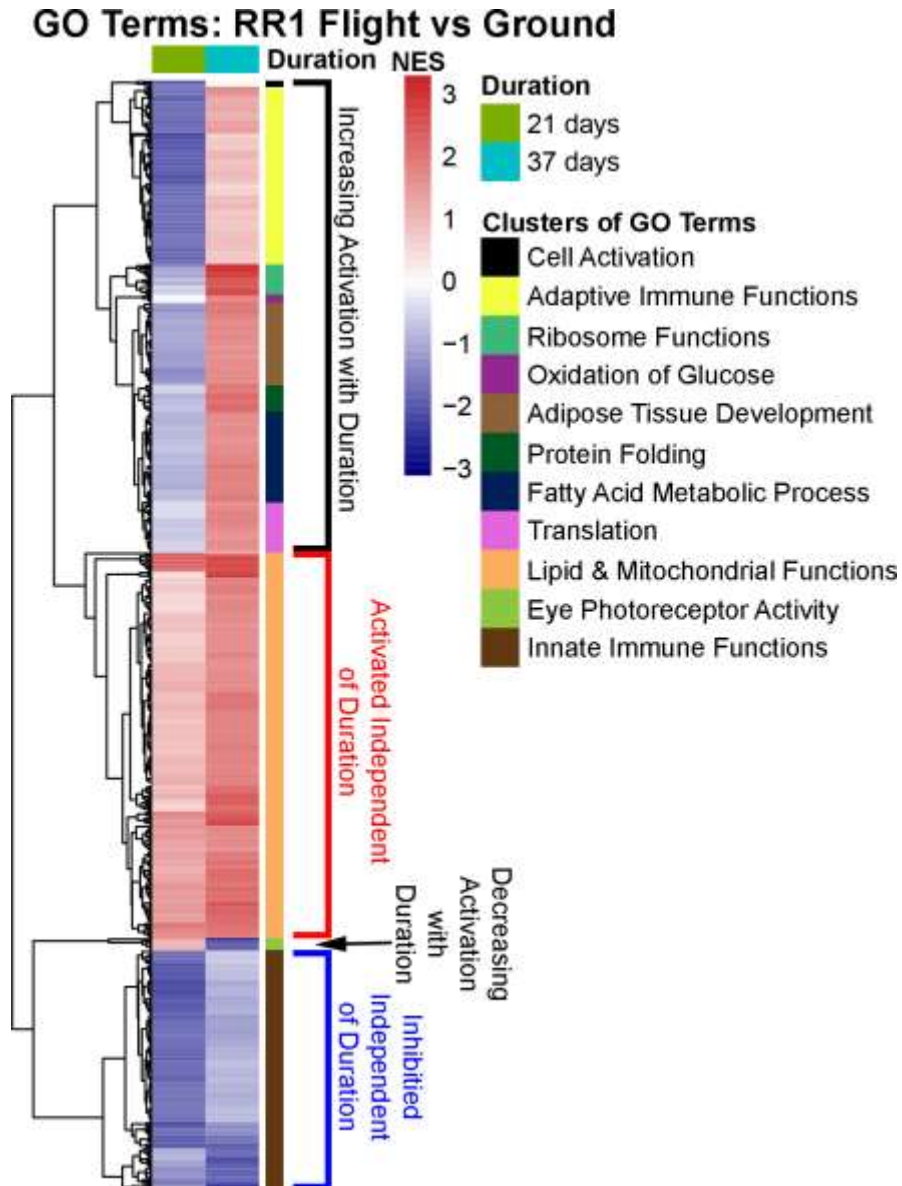
STS135: Liver, Flight vs Ground Controls



GSEA Analysis on RR1 and RR3 Liver Samples Reveals Common Dysregulation with Lipid Related Pathways

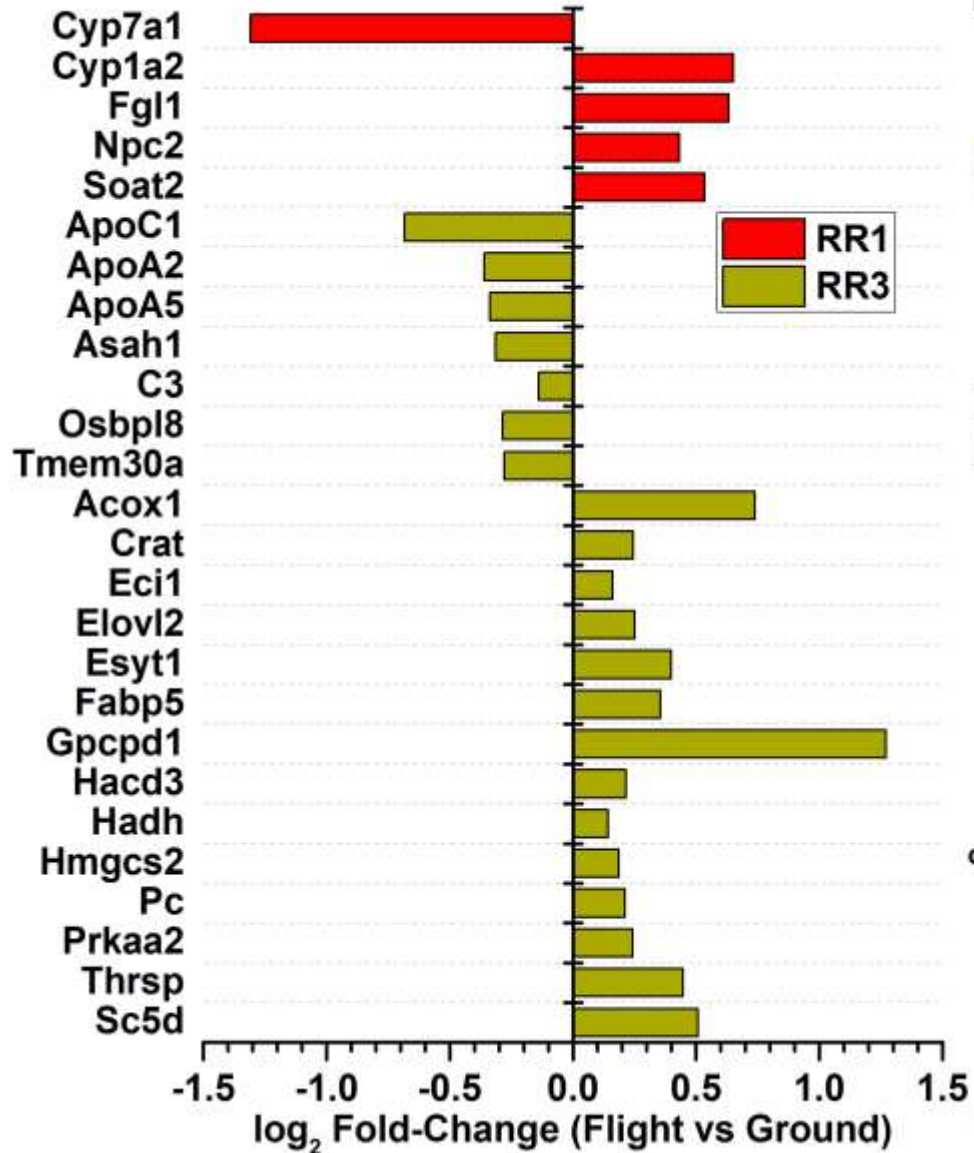




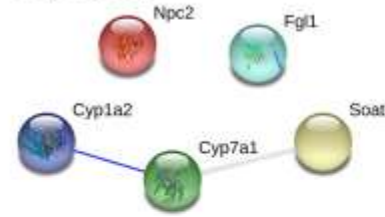


- A set of Pathways Increase with duration in space:
 - The majority of these pathways are related to increases in the adaptive immune system.
 - It has been previously shown that long exposure to the space environment does indeed activate persistent adaptive immune system pathways which will have potential to impact spaceflight associated health risks linked to reactivation of latent herpesviruses and increased incidence of infectious diseases.
 - Oxidation of glucose and adipose tissue development are directly impacted by the adaptive immune system and both have been previously linked with adaptive immune system changes during spaceflight.
 - Protein folding, translation, and ribosome pathways have been directly linked to activation of the adaptive immune system.
- The increase in the fatty acid metabolic process pathways are in agreement with our results in the previous sections indicating an increase in the lipid accumulation as a function of duration in space

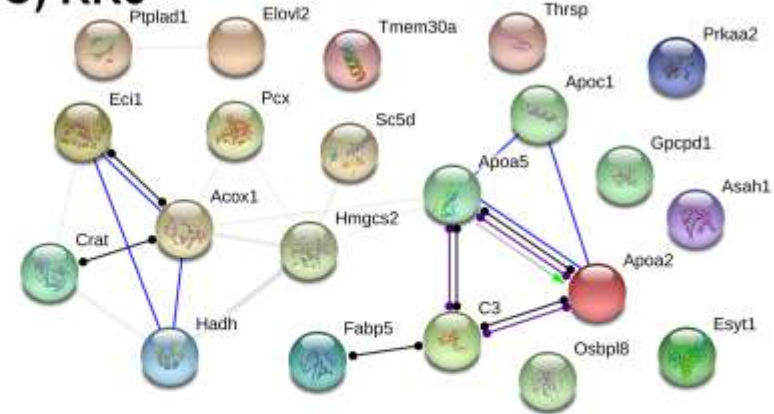
A) Lipid Related Proteins From RR1 and RR3



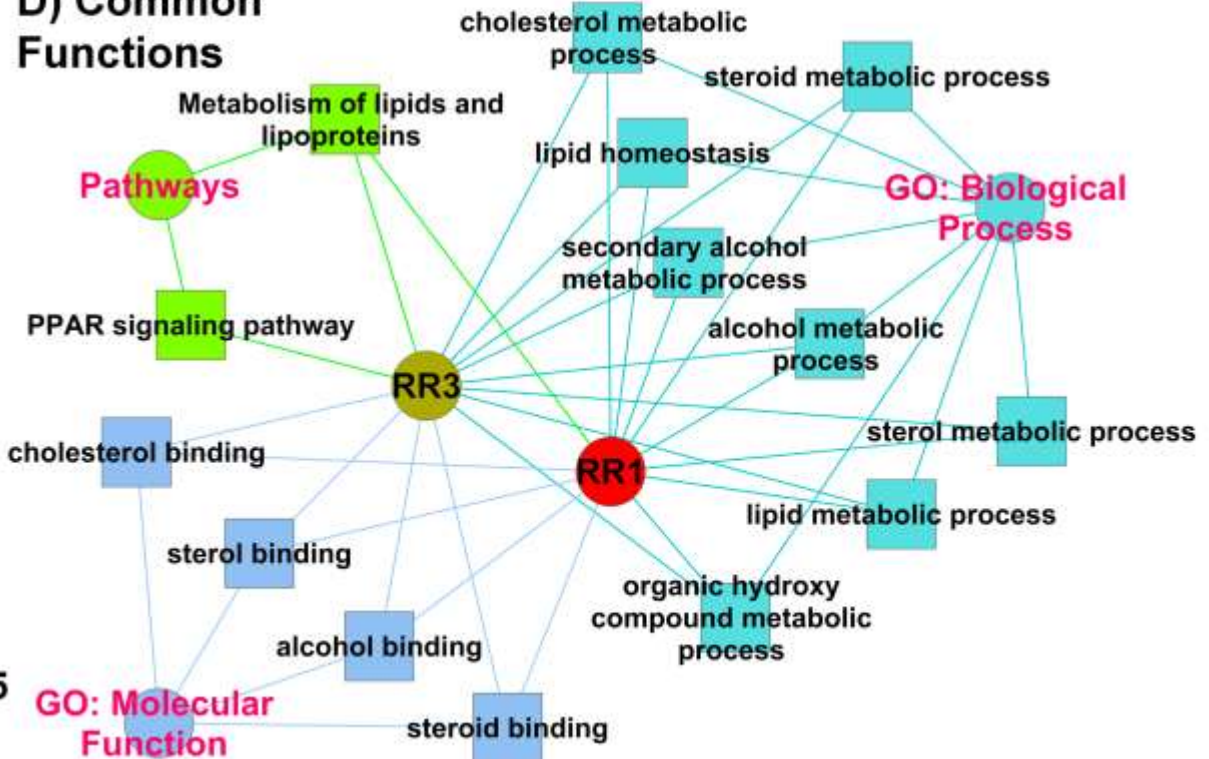
B) RR1

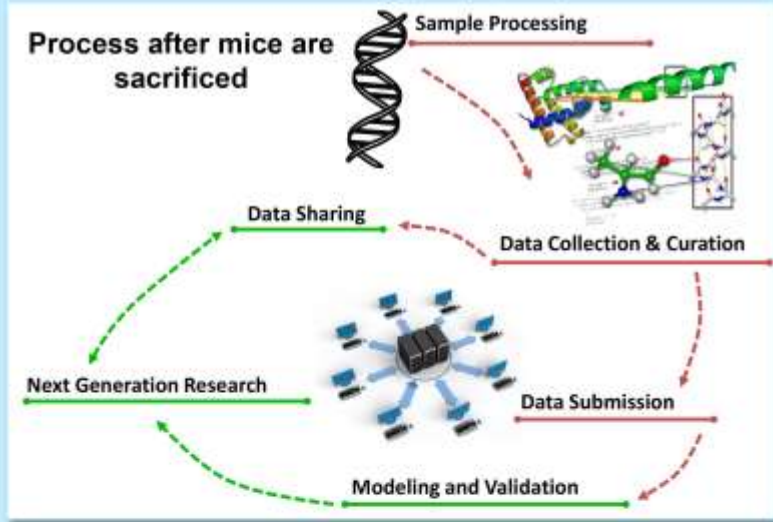


C) RR3



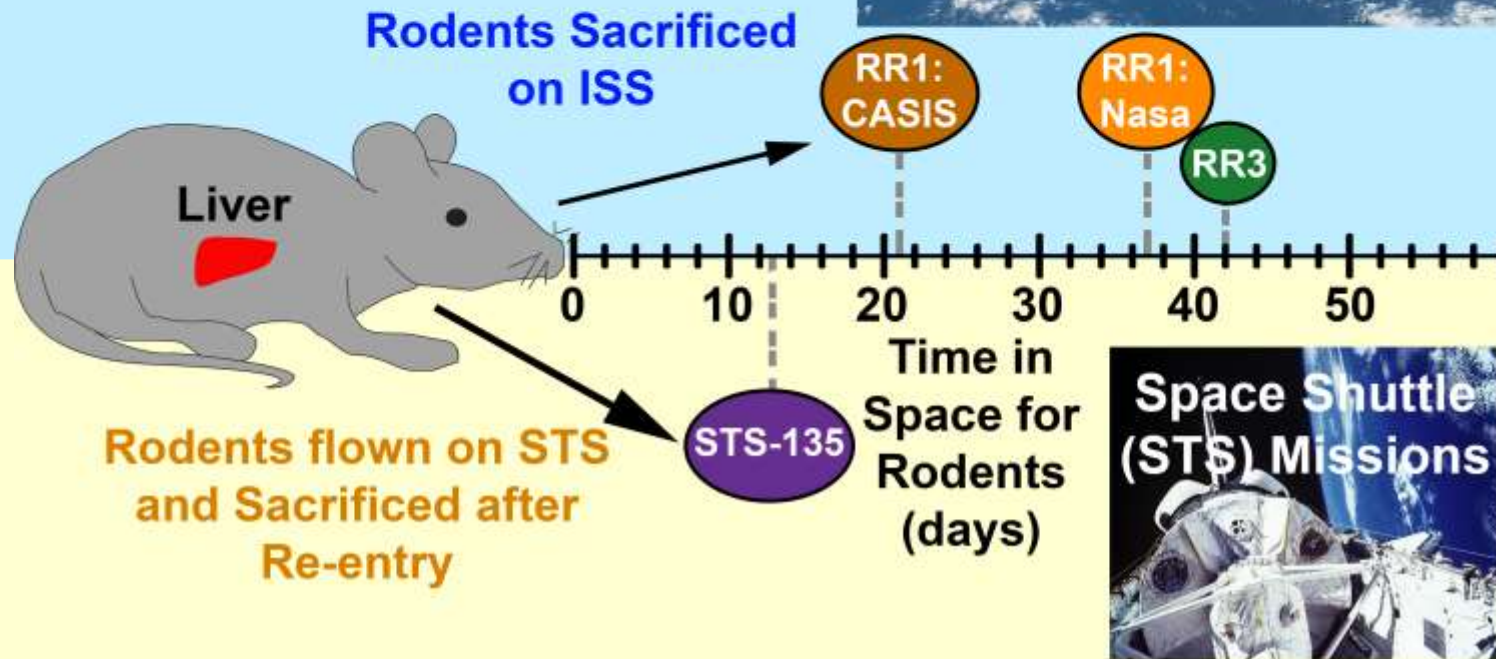
D) Common Functions





Liver after Spaceflight

- ↑ Lipid Metabolism
- ↑ Fatty Acid Metabolism
- ↑ NAFLD

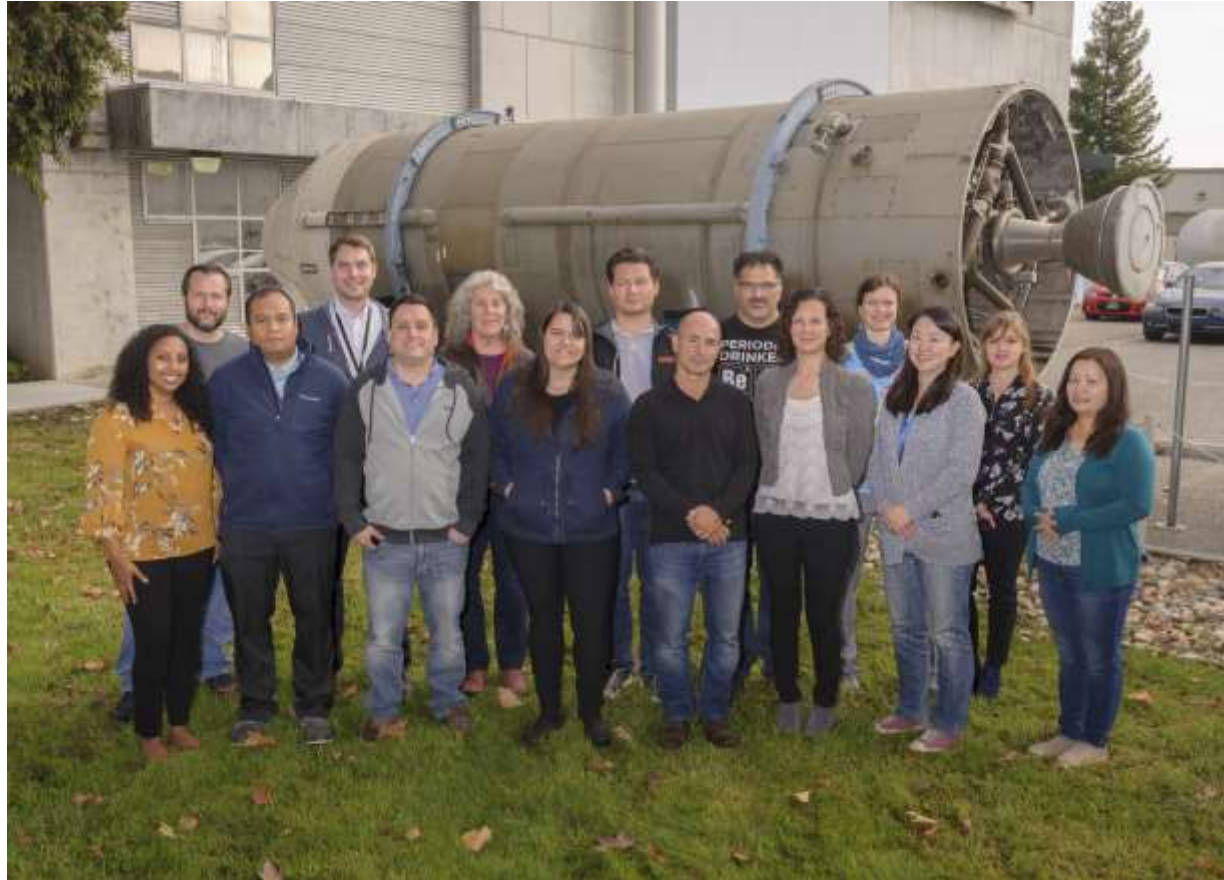




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<https://genelab.nasa.gov/>





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