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

National Aeronautics and Space Administration

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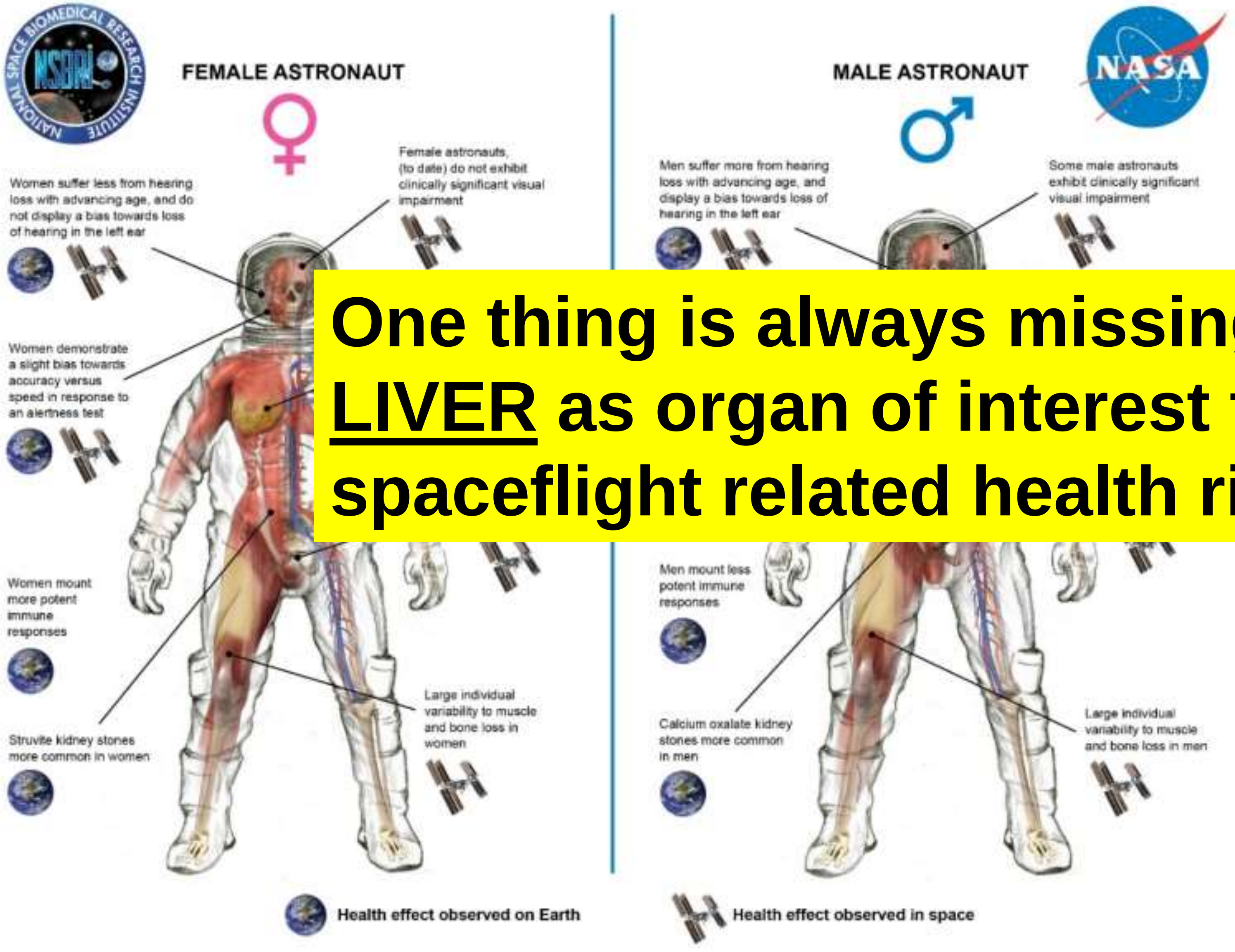
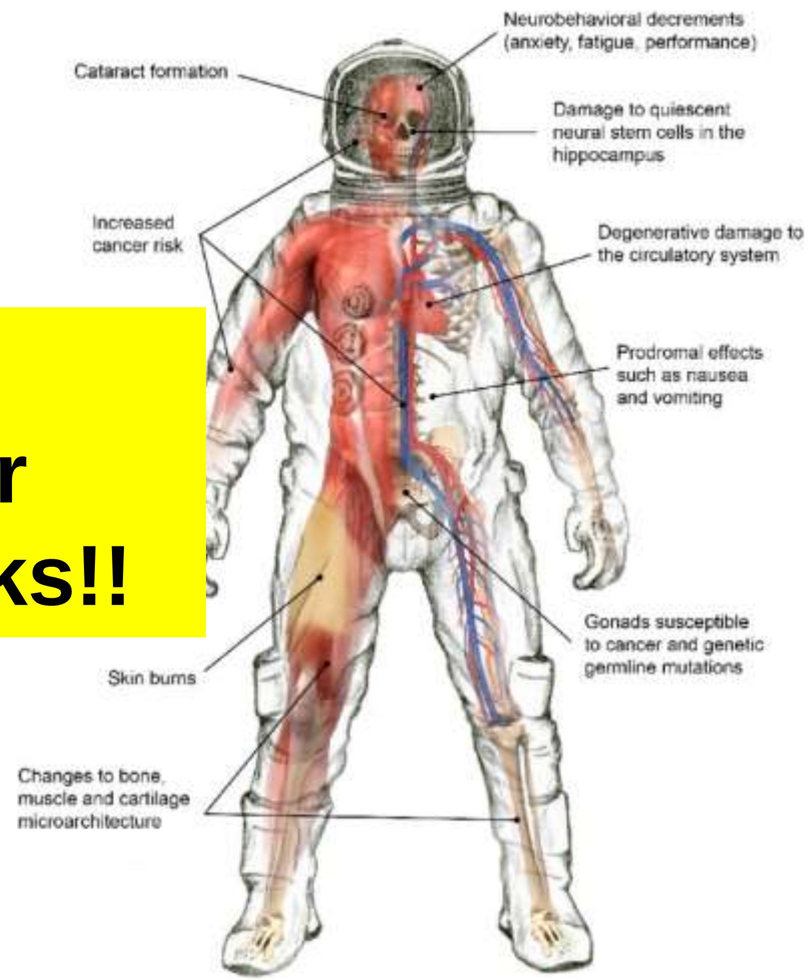
Health Risks On Astronauts in Space



One thing is always missing: <u>LIVER</u> 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;

GeneLab (genelab.nasa.gov)

GeneLab Open Science for Life in Space

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
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LATEST DATA RELEASES

TRANSCRIPTOMICS

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

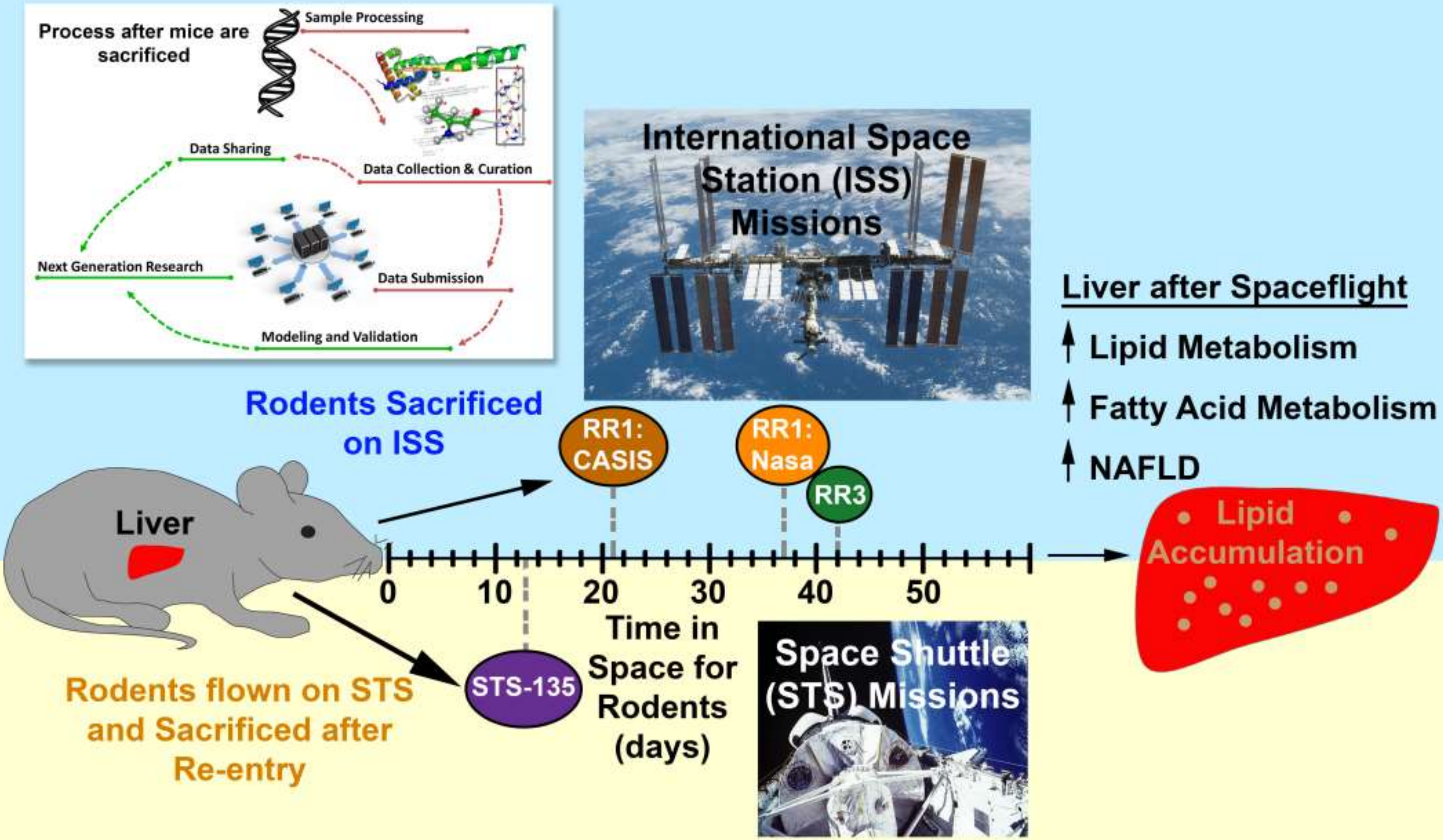
EPIGENOMICS / METAGENOMICS

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

Overview of the Project



Previous Study on Liver from STS-135 Mission Revealed Lipid Accumulation in the Liver

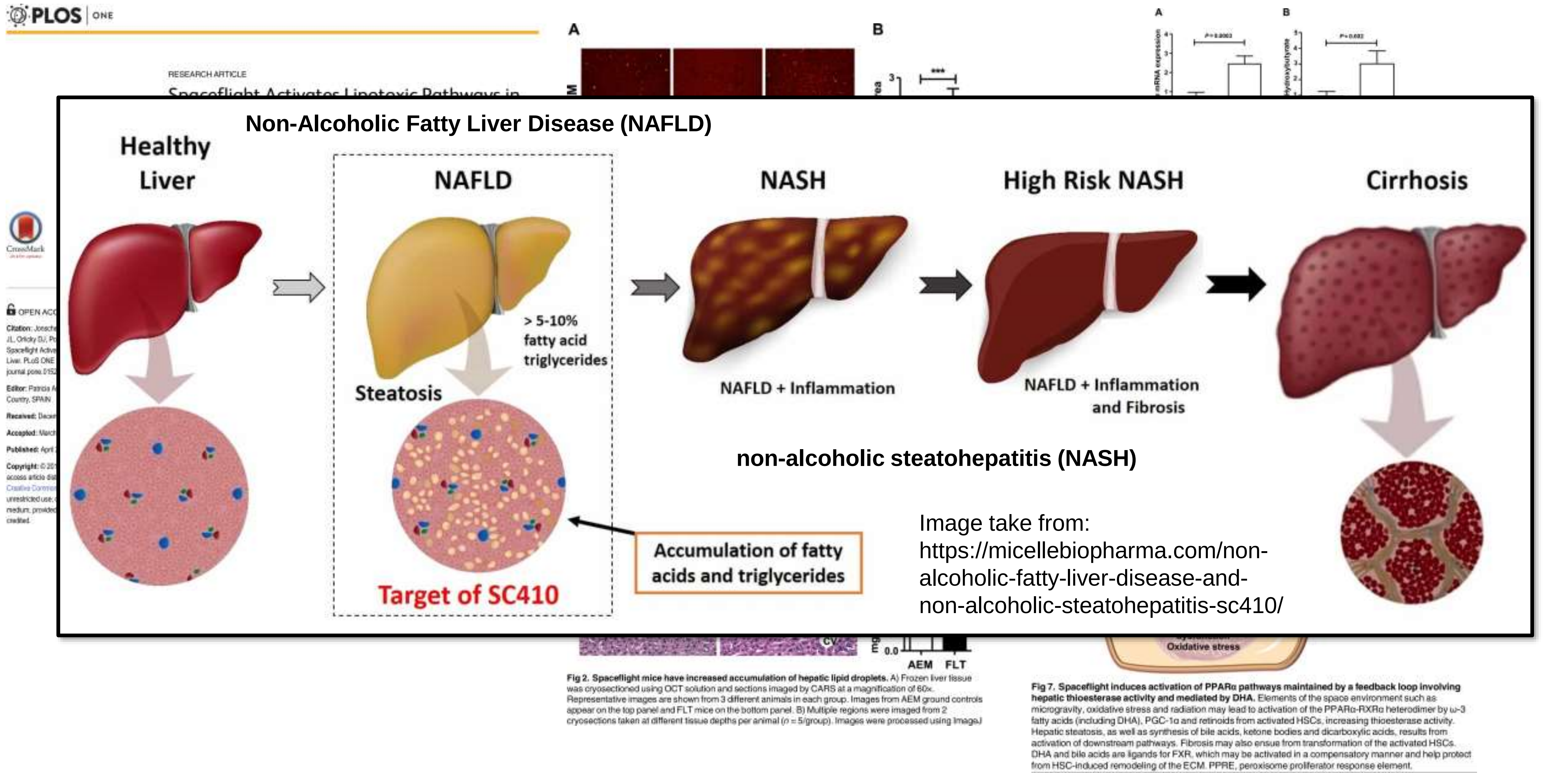
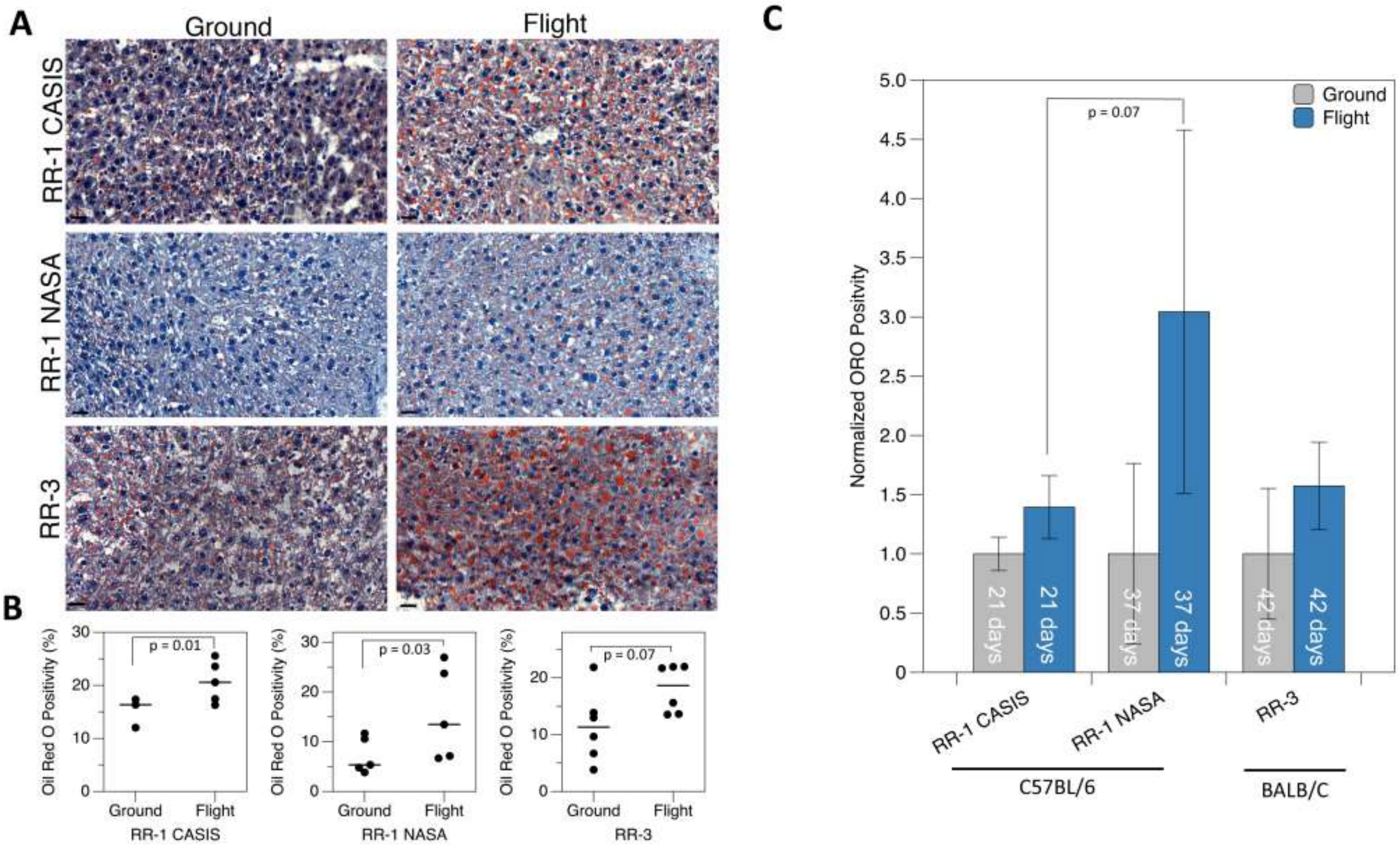
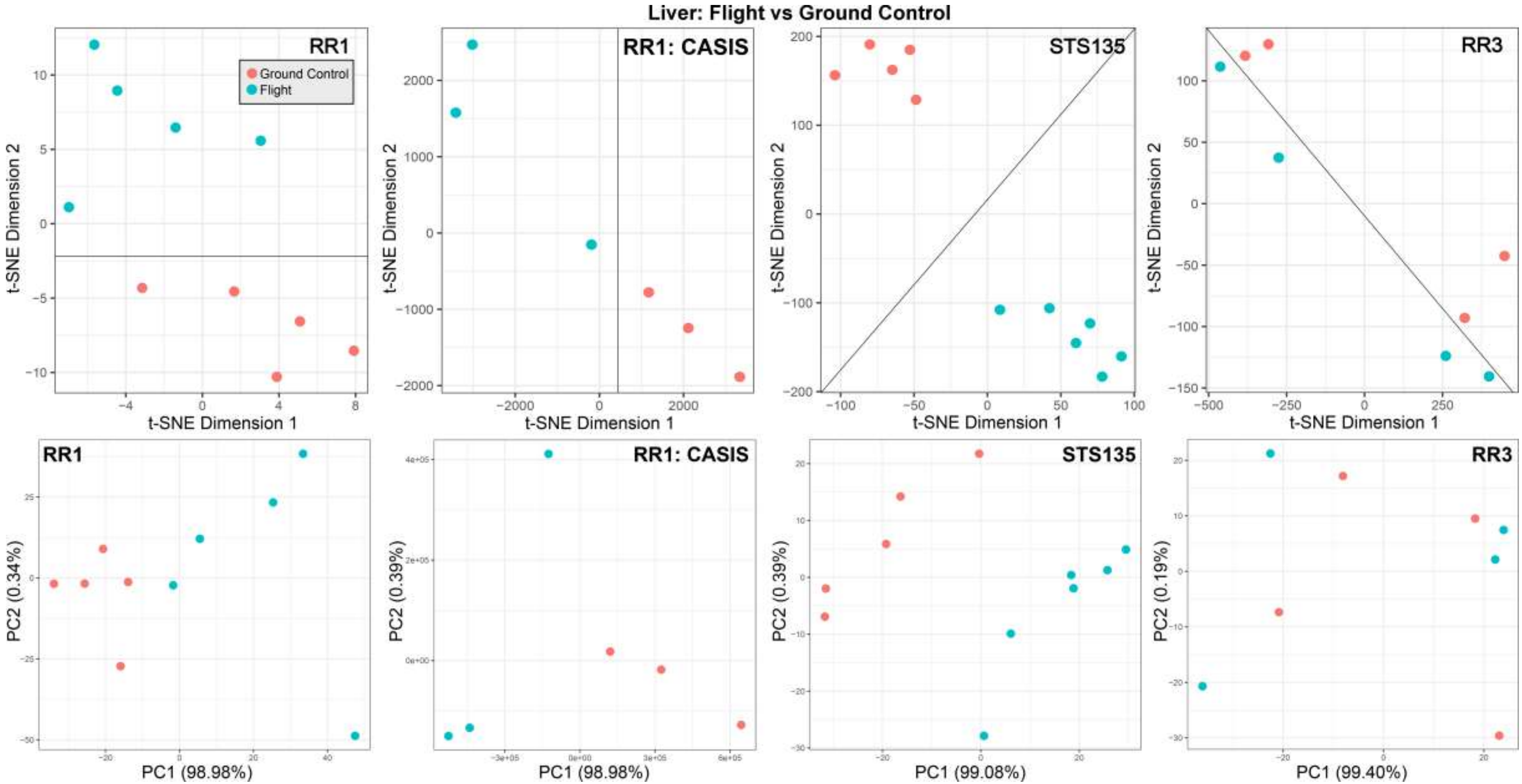


Image take from: https://micellebiopharma.com/non-alcoholic-fatty-liver-disease-and-non-alcoholic-steatohepatitis-sc410/

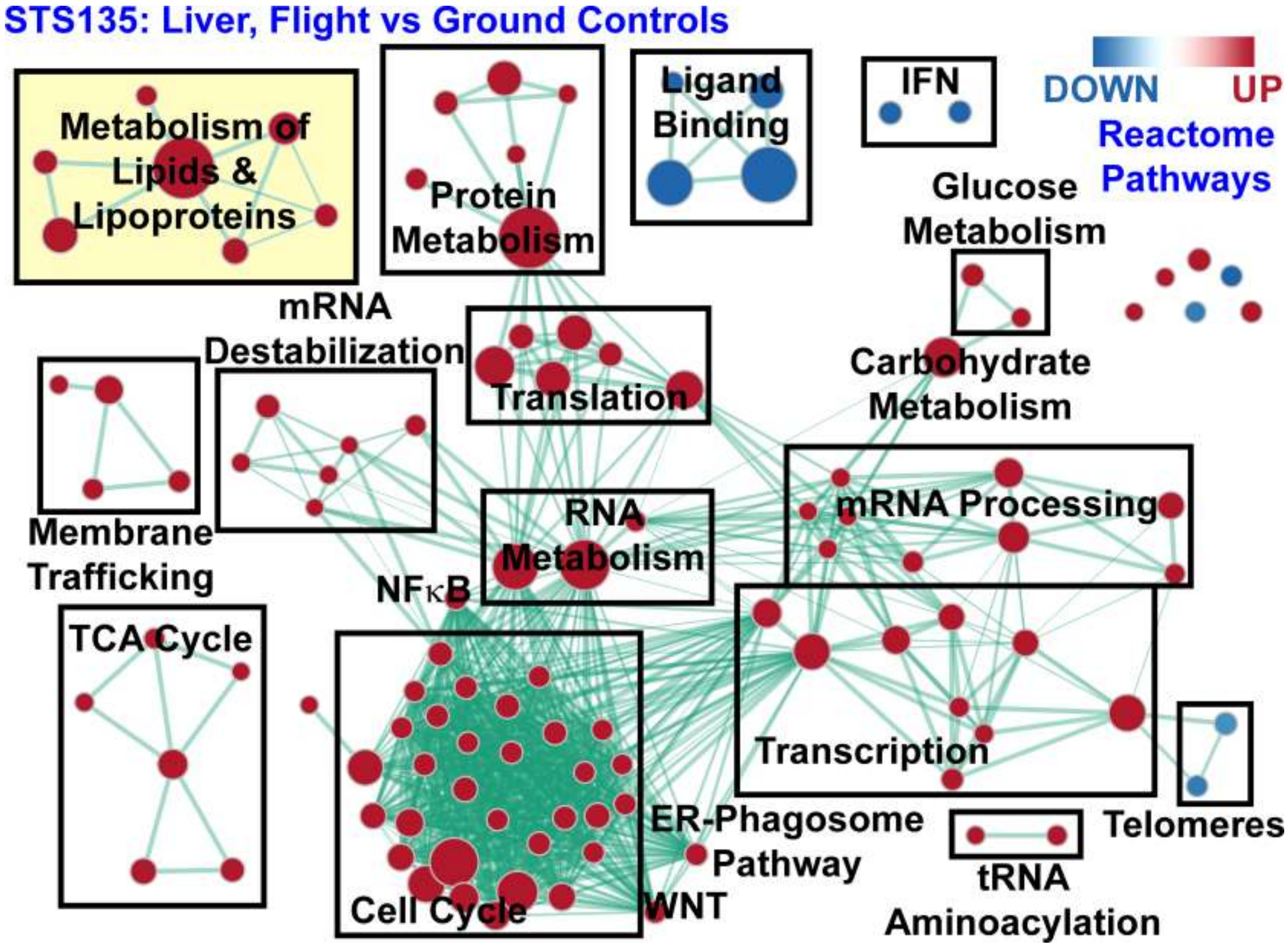
Lipid Accumulation Also Occurs in Livers from More Recent Missions on the ISS



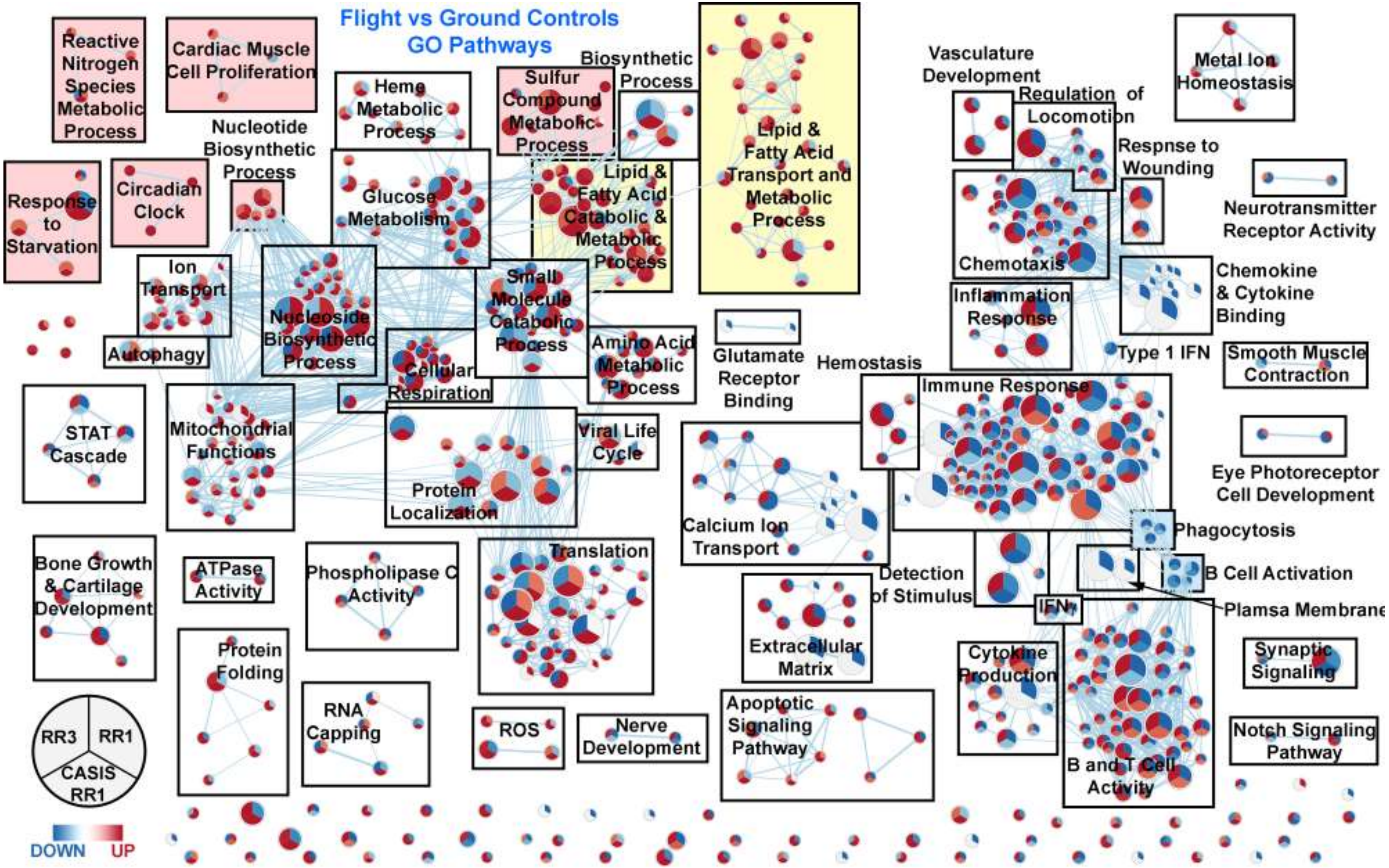
Global View for Transcriptional Factors with Flight vs Ground in the Liver



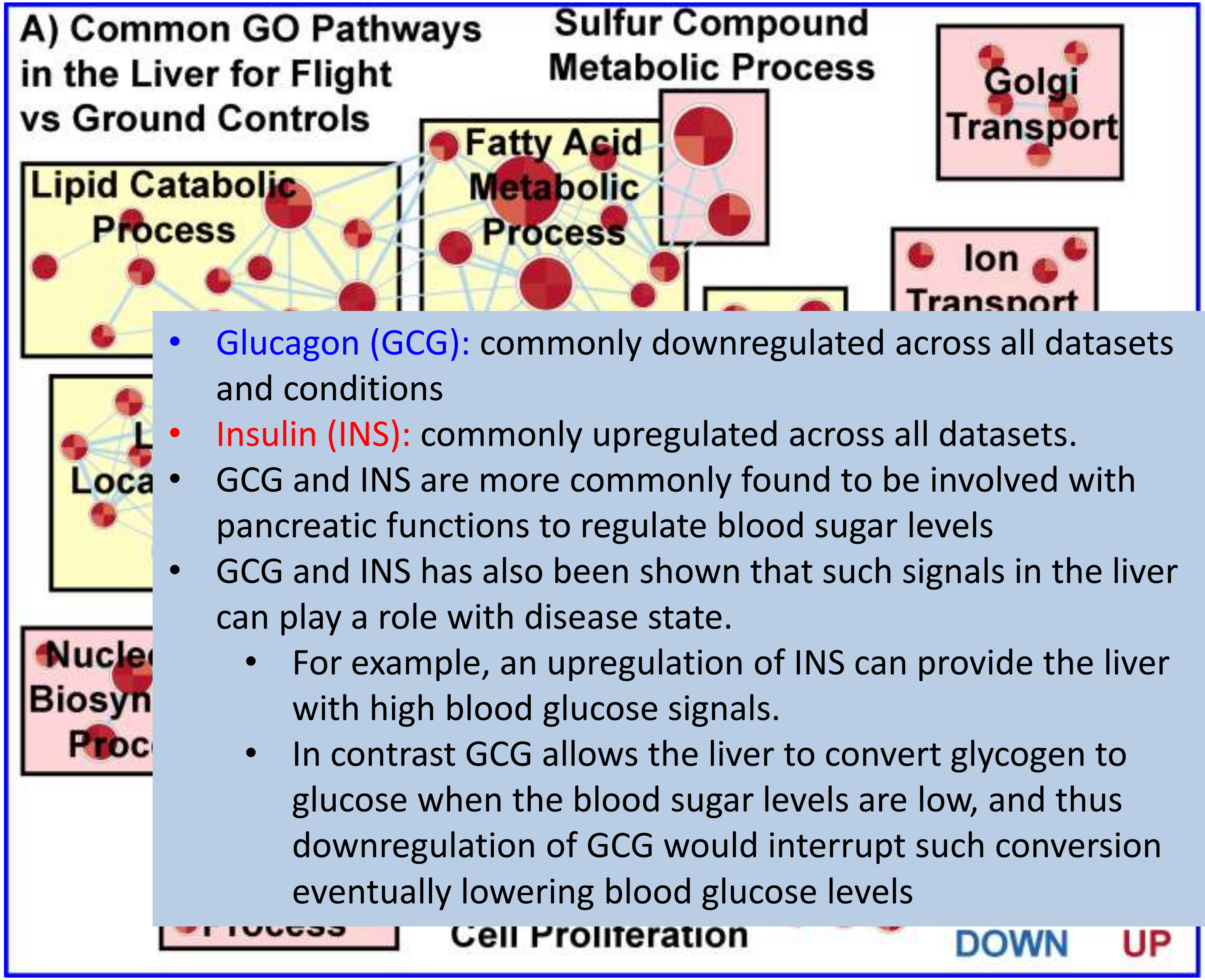
GSEA Analysis on STS-135 Liver Samples Reveals Dysregulation with Lipid Related Pathways



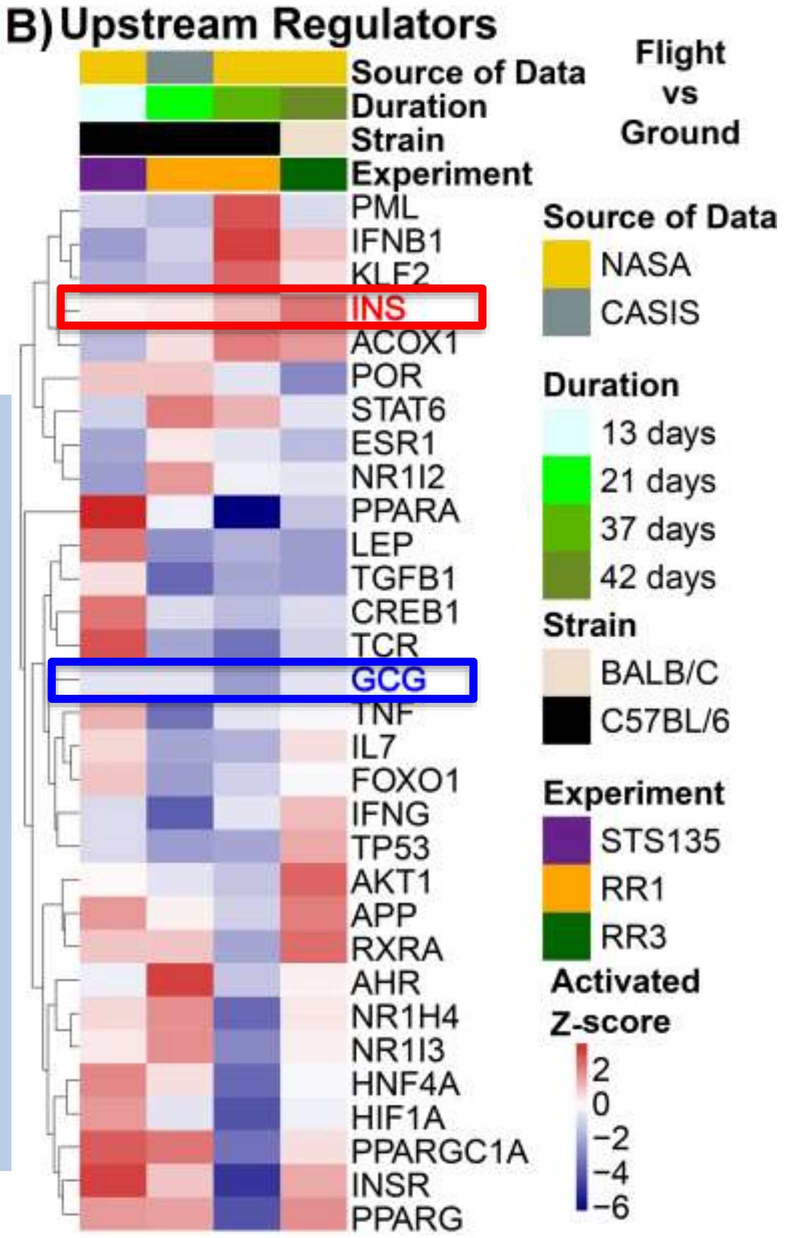
GSEA Analysis on RR1 and RR3 Liver Samples Reveals Common Dysregulation with Lipid Related Pathways



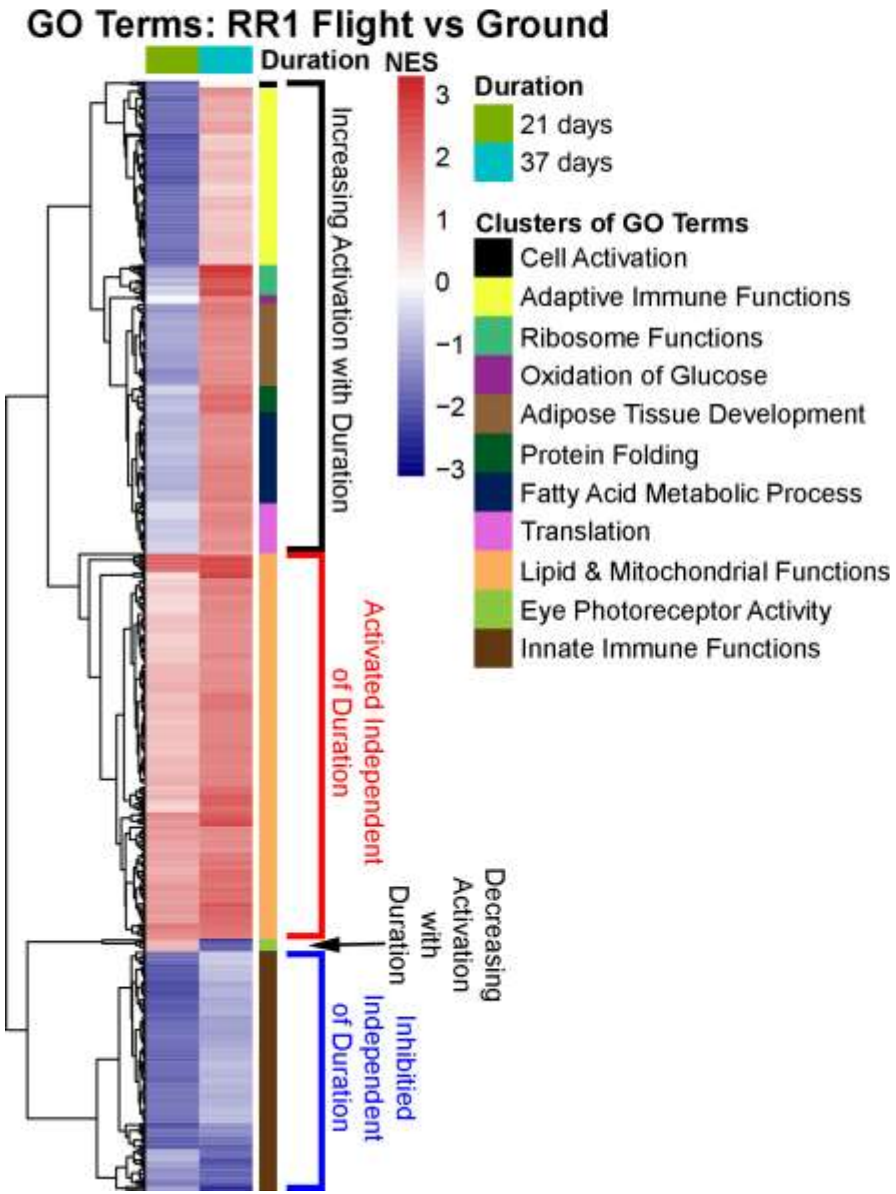
Common Processes and Pathways for all Datasets



- Glucagon (GCG): commonly downregulated across all datasets and conditions
- Insulin (INS): commonly upregulated across all datasets.
- GCG and INS are more commonly found to be involved with pancreatic functions to regulate blood sugar levels
- GCG and INS has also been shown that such signals in the liver can play a role with disease state.
  - For example, an upregulation of INS can provide the liver with high blood glucose signals.
  - In contrast GCG allows the liver to convert glycogen to glucose when the blood sugar levels are low, and thus downregulation of GCG would interrupt such conversion eventually lowering blood glucose levels

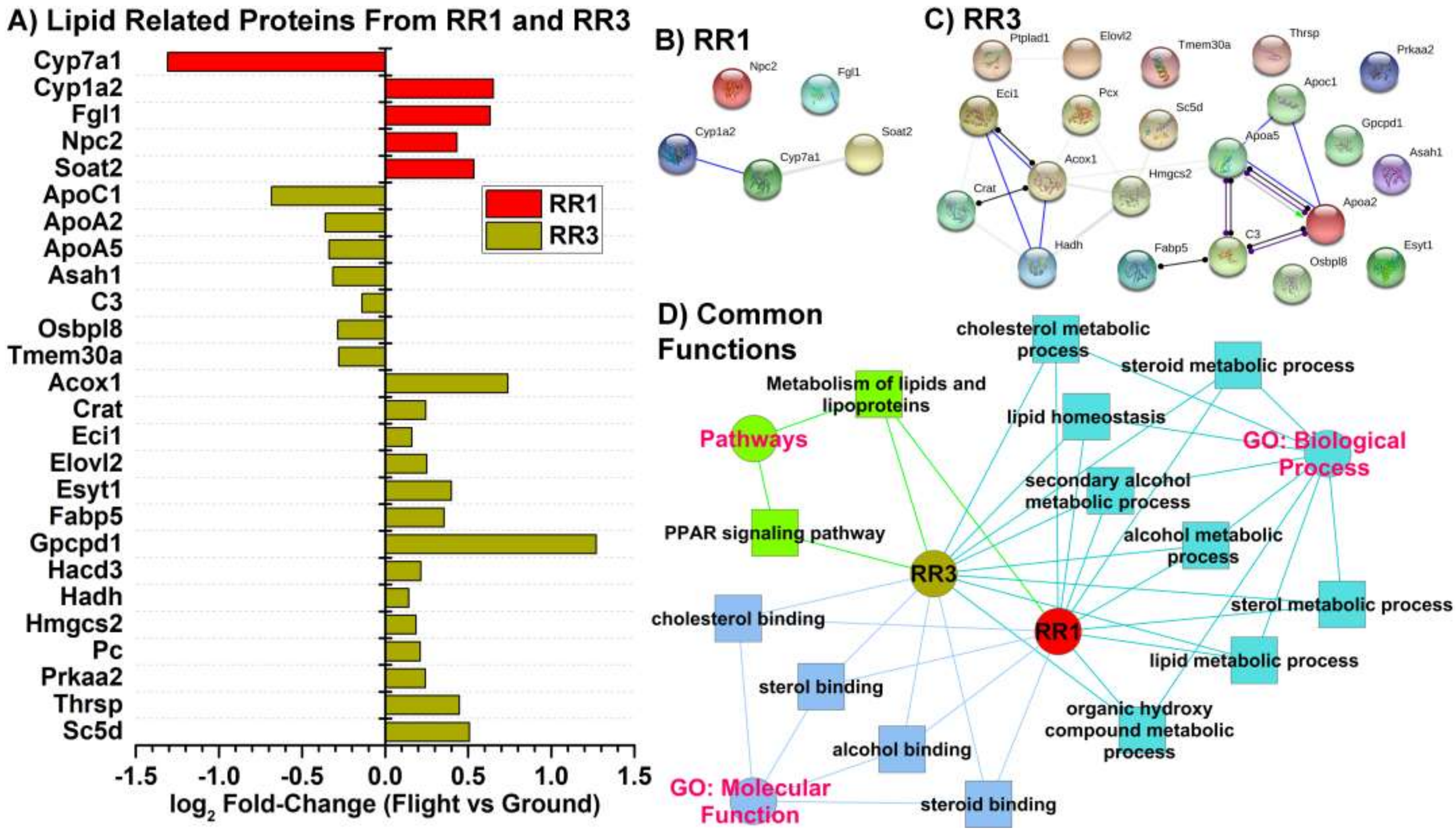


Sapceflight Duration Dependent Changes in the Liver

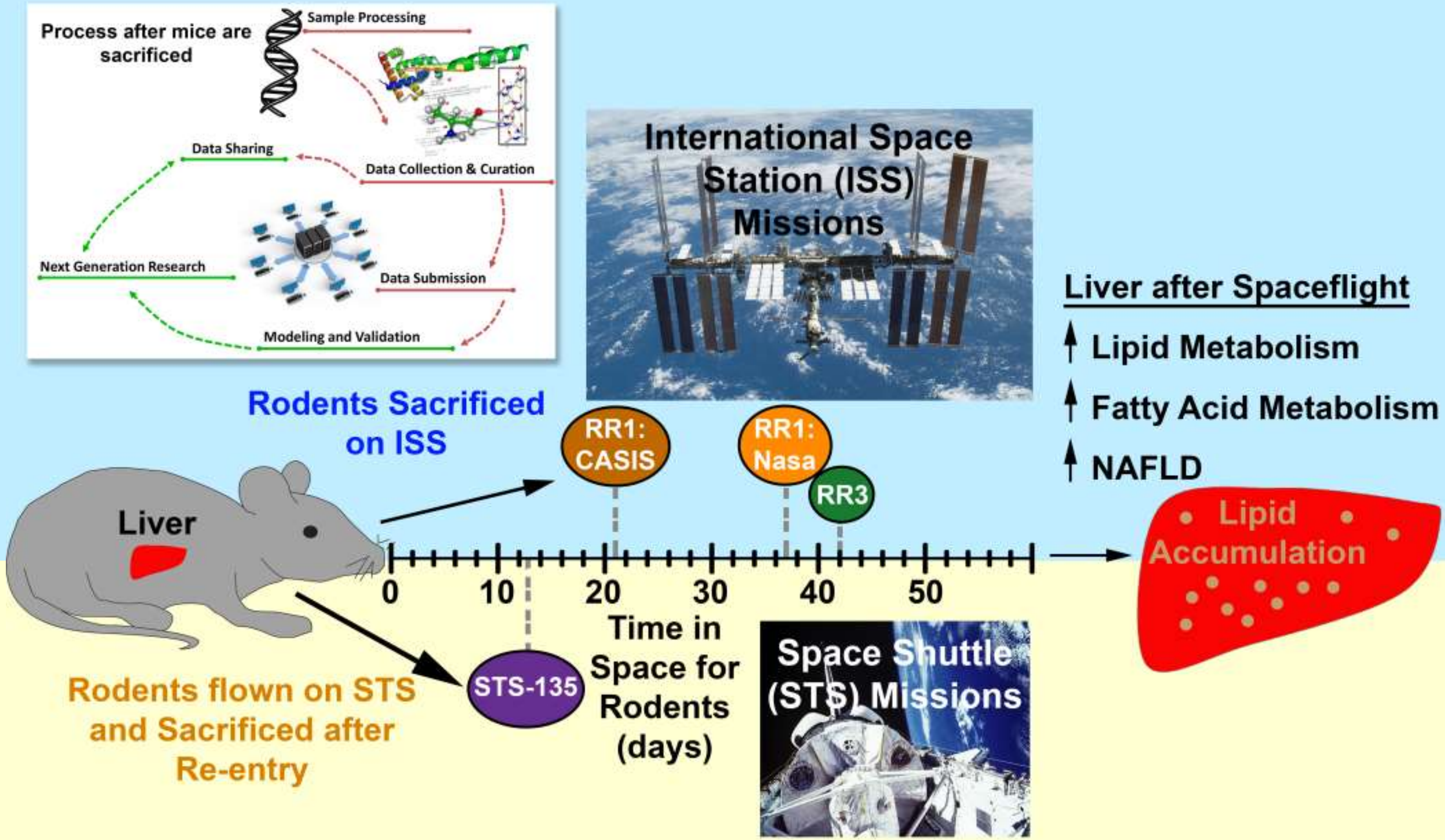


- A set of Pathways Increase with duration in space:
  - The majority of these pathways are related to increases in the adaptive immune system.
  - It has been previously shown that long exposure to the space environment does indeed activate persistent adaptive immune system pathways which will have 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

Proteomics Demonstrate Dysregulation of Lipid Related Proteins



Conclusions



Acknowledgements

https://genelab.nasa.gov/

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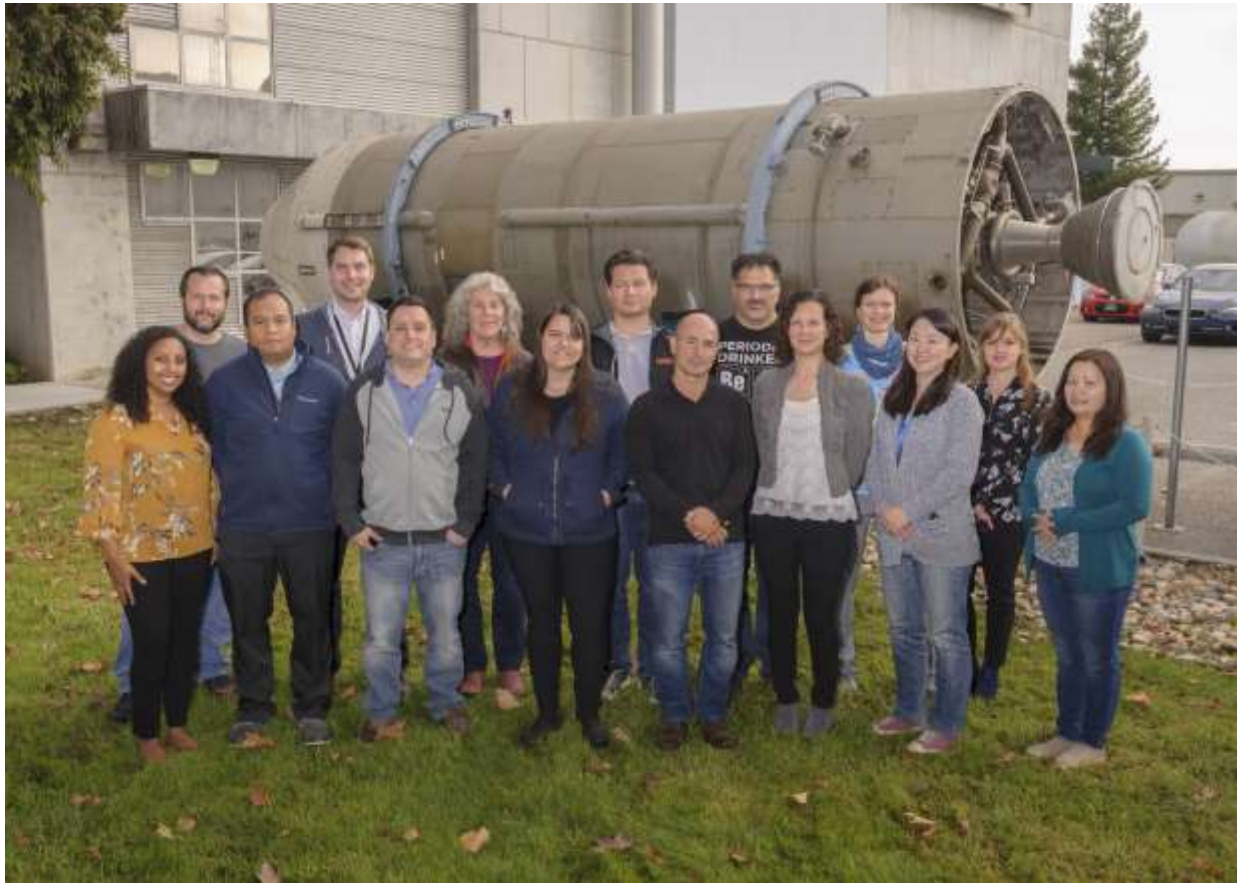

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