Age- and Organ-Specific Lipid Droplet Remodeling under Rapamycin Treatment Revealed by Raman Imaging in Drosophila

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Background

mTOR Signaling Pathway

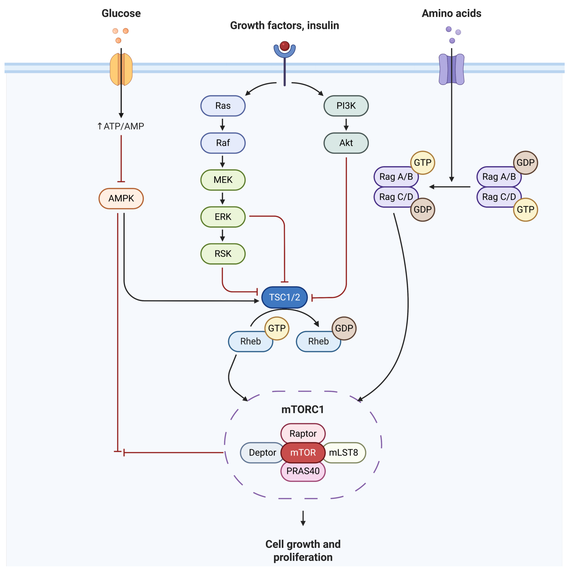


Figure 1. Signaling pathway of the Mechanistic Target of Rapamycin Complex 1 (mTORC1). Rapamycin acutely blocks this complex and inhibits downstream protein (S6K pathway) and lipid (SREBP pathway) synthesis. Rapamycin has been explored for its potential anti-aging and anti-cancer effects and is clinically used as an immunosuppressant in contexts such as transplant medicine.

Objectives

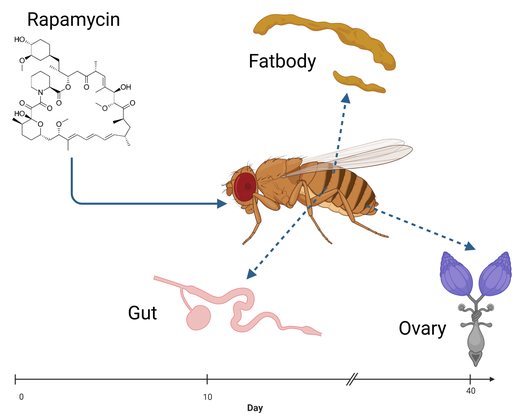
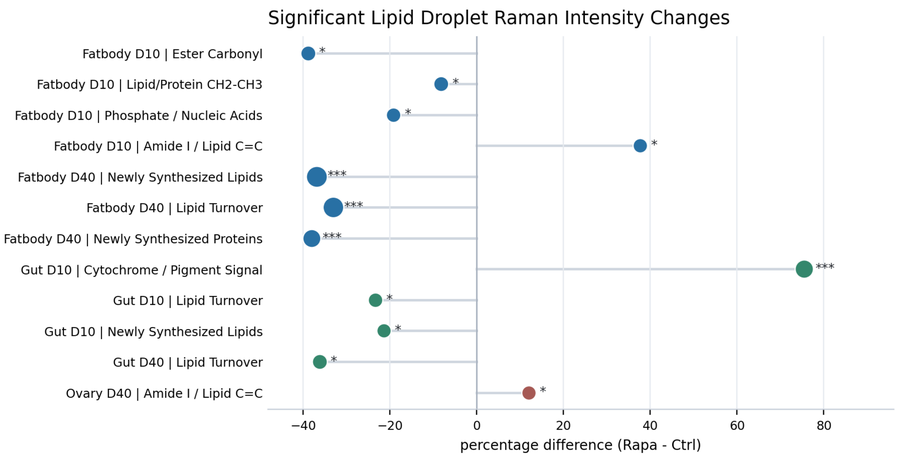


Figure 2. Rapamycin-mediated inhibition of mTORC1 extends lifespan in Drosophila, but its **organ-specific metabolic effects** remain poorly understood.

RESULTS

Figure 4. Raman spectral shape comparison between organs and age groups. The spontaneous Raman spectra are plotted from 400 cm^{-1} to 3200 cm^{-1}, covering the fingerprint region, cell silent region, and CH stretching region with zoomed in peak comparisons showing the differences in peak shift and peak shape.



Wavenumber / Ratio	Biochemical Assignment
1078 cm^{-1}	Phosphate / Nucleic Acids
1120 cm^{-1}	C–C / C–O Stretch
1235 cm^{-1}	Amide III β-Sheet
1260 cm^{-1}	Unsaturated Lipids
1270 cm^{-1}	Amide III / Protein
1300 cm^{-1}	Lipid CH_2 Bending
1335 cm^{-1}	CH_3/CH_2 Deformation
1442 cm^{-1}	Lipid/Protein CH_2–CH_3
1580 cm^{-1}	Cytochrome / Pigment Signal
1655 cm^{-1}	Amide I / Lipid C=C
1745 cm^{-1}	Ester Carbonyl
2142 cm^{-1}	Newly Synthesized Lipids
2180 cm^{-1}	Newly Synthesized Proteins
2853 cm^{-1}	Total Lipids
2930 cm^{-1}	Protein-Rich CH_3
3005 cm^{-1}	Unsaturated Lipids
2142 / 2853	Lipid Turnover
2180 / 2930	Protein Turnover
2853 / 3005	Lipid Saturation Index

Figure 5. Lollipop plot of all significant peak intensity percent changes. All values (except for lipid and protein turnover) were normalized with intensity at 2930 cm^{-1}. Statistical significance was calculated from the Welch t statistic. A threshold of $p < 0.05$ was used to define statistical significance. Significance labels are shown as ns, $p \geq 0.05$; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$; ****$p < 0.0001$.

Experimental Design

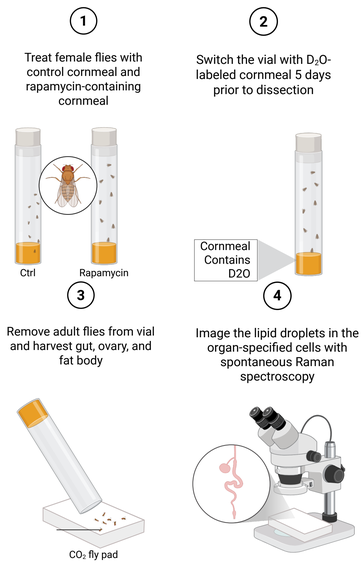


Figure 3. Experimental workflow for raising, dissecting, and imaging the Drosophila.

Conclusion

In D40 fat body, significant reduction in newly synthesized lipids, lipid turnover, and newly synthesized proteins with rapamycin suggests **suppression of biosynthetic activity in the fat body**. The gut also responded, , particularly at D10, with decreased lipid synthesis/turnover markers and a strong increase in a cytochrome/pigment-associated signal, indicating **early gut-specific biochemical remodeling**. In contrast, limited significant changes in ovary samples suggest either weaker sensitivity to rapamycin or greater sample heterogeneity. These results support the hypothesis that **rapamycin remodels lipid droplet composition and metabolic turnover in a tissue- and time-dependent manner**.

Future Directions

Spontaneous Raman spectroscopy is not a 2D mapping of the tissue, thus we might lose some spatial information. In the future, we are planning to use stimulated Raman scattering (SRS), for improved spatial resolution.

Acknowledgements

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