Lipid metabolism and aging: *Diaclyglycerol lipase* regulates lifespan in both *Drosophila* and *C. elegans*

Horng-Dar Wang (汪宏達)

Institute of Biotechnology and Department of Life Science,

National Tsing Hua University, HsinChu, Taiwan 30013

Abstract:

Target of rapamycin (TOR) signaling is a nutrient-sensing pathway controlling metabolism and lifespan. Although TOR signaling can be activated by phosphatidic acid (PA), a metabolite of diacylglycerol (DAG) processed by DAG kinase, how the genetic regulation of DAG metabolism influences lifespan remains unknown. In addition to being metabolized to PA, DAG can also be converted to 2-arachidonoyl-*sn*-glycerol by diacylglycerol lipase (DAGL). Here, we report that in both *Drosophila* and *C. elegans,* overexpression of *diacylglycerol lipase* (*DAGL*/*inaE*/*F42G9.6*) or knockdown of *diacylglycerol kinase* (*DGK*/*rdgA*/*dgk-5*) extends lifespan and enhances oxidative stress resistance by reducing TOR signaling, which subsequently lowers levels of phosphorylated S6 kinase (p-S6K). *DAGL*/*F42G9.6* mutants show reduced lifespan, lower tolerance to oxidative stress and elevated levels of p-S6K. Genetic interaction studies support the notion that DAG metabolism interacts with TOR and S6K signaling to affect lifespan and oxidative stress resistance. Together, our results demonstrate that *DAGL*/*F42G9.6* regulates lifespan and oxidative stress response through TOR signaling in both *Drosophila* and *C. elegans*. Our findings add insights into the genetic regulation of DAG metabolism in modulating lifespan and oxidative stress response.