Sánchez-Blanco, A., Rodríguez-Matellán, A.G., Reis-Sobreiro, M., Sáenz-Narciso, B., Cabello, J., Mohler, W.A., and Mollinedo, F. (2014). *Caenorhabditis elegans* as a platform to study the mechanism of action of synthetic antitumor lipids. *Cell Cycle* 13, 3375-3389.

Drugs capable of specifically recognizing and killing cancer cells while sparing healthy cells are of great interest in anti-cancer therapy. An example of such a drug is edelfosine, the prototype molecule of a family of synthetic lipids collectively known as antitumor lipids (ATLs). A better understanding of the selectivity and the mechanism of action of these compounds would lead to better anticancer treatments. Using Caenorhabditis elegans, we modeled key features of the ATL selectivity against cancer cells. Edelfosine induced a selective and direct killing action on C. elegans embryos, which was dependent on cholesterol, without affecting adult worms and larvae. Distinct ATLs ranked differently in their embryonic lethal effect with edelfosine > perifosine > erucylphosphocholine >> miltefosine. Following a biased screening of 57 C. elegans mutants we found that inactivation of components of the insulin/IGF-1 signaling pathway led to resistance against the ATL edelfosine in both C. elegans and human tumor cells. This paper shows that C. elegans can be used as a rapid platform to facilitate ATL research and to further understand the mechanism of action of edelfosine and other synthetic ATLs.