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Differential role of Fus3p MAPK and its phosphorylation target Far1p in the cell death induced by an α-pheromone-like peptide in *Saccharomyces cerevisiae*

Paula Martinell García

Instituto de Fisiología Celular, UNAM, Mexico City

The Iztli peptide 1 (IP-1) is a hunter-killer peptide with 19 residues: 13 residues correspond to the α -pheromone sequence from *Saccharomyces cerevisiae* and the other 6 residues provide the 19mer peptide with antimicrobial activity. In this design, one single functional domain (antimicrobial activity) combines two activities. This renders a peptide with an emerging property: to kill MATa cells from *S. cerevisiae*. While high concentrations of α -pheromone have proven to induce the cell death of MATa cells, IP-1 at lower concentration kills many more cells than the pheromone; moreover the cell death induced by Iztli seems to be independent from apoptosis-like death as opposed to the α -pheromone(1).

Screening for every gene deletion involved in the α -pheromone signaling pathway, we found that the genes coding for the MAPK cascade proteins protect from the cell death induced by IP-1 with different degrees. *STE11* (MAPKKK) and *STE7* (MAPKK) absence have full protective effect against IP-1 action, while *FUS3* (MAPK) absence protects only partially. Fus3p when active, phosphorylates/activates Far1p, the latter protein is responsible for cell cycle arrest. Despite Δ FUS3 has a partial protection against IP-1 induced death, cells lacking *FAR1* recover a phenotype similar to D*STE11* and D*STE7*. By contrast, all these genes have a degree of protection against the cell cycle arrest induced by the α -pheromone that significantly differ from the cell death protection against IP-1. These results indicate that IP-1 may be able to differently activate the MAPK pathway. We are currently testing this new mechanism of activation with double deletion mutants and with Western Blot assays.

Biography:

Paula Martinell studied Biology in the Universidad Nacional Autonoma de Mexico (UNAM) in Mexico City and is currently at the end of the 2nd year of her Master's studies on Biochemistry at the same university. The laboratory she is working at is involved in two main research branches: the first one regards the study of protein structure through a bioinformatic approach, the second consists on determining the mechanisms that the Iztli peptide 1 triggers in the MATa yeast cells.

laxmita666@gmail.com