

Deciphering the mechanisms underlying bovine milk lactoferrin anticancer activity using yeast and cancer cell lines as complementary models

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Lactoferrin (Lf) is a milk derived iron-binding protein that exhibits a broad range of interesting biological activities, from which its anticancer and antifungal activities stand out. Our group has been elucidating the mechanisms and identifying the molecular targets underlying Lf anticancer/antifungal activities in order to improve its therapeutic efficacy and rational application. Indeed, we previously demonstrated that Lf triggers a mitochondrial and caspase-dependent regulated cell death in *Saccharomyces cerevisiae* (1). Moreover, we found that Lf selectively induces apoptosis in highly metastatic cell lines displaying the proton pump V-ATPase at the plasma membrane (2). However, much work is needed to further characterize Lf mechanisms of action. In the present work, we show how functional genomic approaches using yeast deletion mutants provided new insights on the activity of Lf against yeast that were then validated in human cancer cell lines. Results will be discussed in an integrated manner regarding their contribution towards understanding the molecular basis of Lf anticancer activity. In addition, this study highlights the great potential of yeast as a model to uncover mechanisms of action occurring in the more complex human cells.

References

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- (2) Pereira CS, Guedes JP, Gonçalves M, Loureiro L, Castro L, Gerós H, Rodrigues LR, Côrte-Real M. (2016) Lactoferrin selectively triggers apoptosis in highly metastatic breast cancer cells through inhibition of plasmalemmal V-H⁺-ATPase. *Oncotarget*. 7(38):62144-62158. doi: 10.18632/oncotarget.11394.