Heterocyclic chalcone derivatives: Synthesis and biological activity evaluation

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Introduction: Natural chalcones have been intensively studied for their wide range of biological activities, namely antitumor.1 Possessing two electrophilic reactive centers at α,β-unsaturated ketone group, chalcone derivatives can participate in addition reactions leading to the synthesis of promising bioactive compounds with a more rigid structure, like isoxazoles and pyrazoles.2

Methods: Chalcones were synthesized by base catalysed Claisen Schmidt condensation via microwave assisted organic synthesis (MAOS). The antiproliferative activity was assessed using sulforhodamine B assay.3

Results: Seventeen chalcone derivatives were synthesized and identified as having in vitro growth inhibitory activity on three human tumor cell lines from breast, lung and melanoma (MCF-7, NCI-H460, and A375-C5).

Conclusion: Most of the synthesized chalcones revealed to be promising growth inhibitors of human tumor cell lines. The molecular mechanisms involved in their antiproliferative effect are being evaluated.

Acknowledgements: This research was partially supported through national funds provided by FCT, ERDF and COMPETE under the Strategic Funding UID/Multi/04423/2013, and the projects PTDC/MAR-BIO/4694/2014 (POCI-01-0145-FEDER-016790), PTDC/DTPPTO/1981/2014 (POCI-01-0145-FEDER-016581), and PTDC/AAGTCC/0739/2014 (POCI-01-0145-FEDER-016793) in the framework of the programme PT2020 as well as by the project INOVMAR-Innovation and Sustainability in the Management and Exploitation of Marine Resources (NORTE-01-0145-FEDER-000035, within Research Line NOVELMAR), supported by NORTE 2020, under the PORTUGAL 2020 Partnership Agreement, through the ERDF. Patrícia M.A. Silva is a PhD fellowship holder from FCT (SFRH/BD/90744/2012).

References

http://dx.doi.org/10.1016/j.pbj.2017.07.115

A posttranslational modification in histones as prognostic/predictive marker in Estrogen-Positive Breast Cancer

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Aim: This work aims to evaluate H3K27me3 expression in luminal-like breast tumors, using immunohistochemistry assay, to assess the prognostic value of this epigenetic alterations in estrogen positive breast cancer (BrC).

Introduction: BrC is the second most incident cancer worldwide. In Portugal, in 2012, BrC was simultaneously the leading cancer in incidence and mortality in women.1 Around 70% of all BrC are hormone-receptor positive, that is the major part of breast tumors is luminal-like.2 H3K27m3 is a gene repression marker and is associated with gene silencing, playing a crucial role in cell proliferation and differentiation.3 H3K27m3 may have some clinical value in several types of cancer since it can be used as a biomarker. This histone modification has been associated with poor prognosis of some BrC subtypes.2

Methods: It was used a cohort of BrC patients of the Portuguese Oncology Institution of Porto (IPO-Porto), diagnosed between 1994 and 2002. A total of 102 luminal-like tumor cases were assessed by immunohistochemistry, to H3K27me3 expression. To verify the prognostic value of H3K27me3 levels, Cox regression with a log rank test was performed for both disease-specific and disease-free survival.

Results: Through the result analysis, it was established that only tumor grade (p = 0.021) was significant associated with disease-specific survival. Nevertheless, both luminal subtype (p = 0.016) and H3K27me3 expression (p = 0.012) were significantly associated with disease-free survival. Indeed, H3K27me3 high expression is associated with higher recurrence risk, especially in Luminal A.

Conclusion: We could confirm the prognostic value of H3K27me3 expression in luminal A subtype BrC patients. Therefore, higher H3K27m3 expression in luminal A tumors is associated with a greater probability of recurrence. However, studies in larger cohorts are mandatory to validate its clinical utility.

Acknowledgements: This study was funded by a grant of the Research Centre of Portuguese Oncology Institute of Porto (CI-IPOP-74-2016).

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