Ps207

Heterocyclic chalcone derivatives: Synthesis and biological activity evaluation

C. Machado 1,*, P. Pinto 1, P. Silva 3,4,5, D. Almeida 3, J. Moreira 1,8, M. Pinto 1,2,3, H. Bousbaa 5,6, H. Cidade 1,6

1 Laboratório de Química Orgânica e Farmacêutica, Departamento de Ciências Químicas, Faculdade de Farmácia, Universidade do Porto, Portugal
2 Laboratório de Química Farmacêutica, Faculdade de Farmácia, Universidade de Coimbra, Portugal
3 Center for Biomedical Research, CBMR, University of Algarve, Faro 8005–139, Portugal
4 Departamento Ciências Biomédicas e Medicina, University of Algarve, Faro, Portugal
5 CESP, Instituto de Investigação e Formação Avançada em Ciências e Tecnologias da Saúde, INFACS, 4585-116 Gandra PRD, Portugal
6 Centro Interdisciplinar de Investigação Marina e Ambiental (CIMAR), Universidade do Porto, Portugal
E-mail address: ccmmariana3@hotmail.com (C. Machado).


Introduction: Natural chalcones have been intensively studied for their wide range of biological activities, namely antitumor. Possessing two electrophilic reactive centers at C=O-un saturated 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. Methods: Chalcones were synthesized by base catalysed Claissen Schmidt condensation via microwave assisted organic synthesis (MAOS). The antiproliferative activity was assessed using sulforhodamine B assay. 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/DTPFTO/1981/2014 (POCI-01-0145-FEDER-016581), and PTDC/AAGTEC/0739/2014 (POCI-01-0145-FEDER-016793) in the framework of the programme PT2020 as well as by the project INNOVMAR-Innovation and Sustainability in the Management and Exploitation of Marine Resources (NORTE-01-0145-FEDER-000305, within Research Line NOVELMAR), supported by NORTE 2020, under the PORTUGAL 2020 Partnership Agreement, through the ERDF. Patricia M.A. Silva is a PhD fellowship holder from FCT (SRH/Bd/90744/2012).

References

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

Ps209

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

S. Lobo 1,2,*, M. Fontes-Sousa 2,3, S. Salta 2, P. Lopes 2,4, J. Lobo 2,4, S. Sousa 3, R. Henrique 2,4,5, C. Jerónimo 1,5

1 Faculty of Science – University of Porto (FCUP-UP), Porto, Portugal
2 Cancer Biology and Epigenetics Group, IPO Porto Research Center (CI-IPOP), Portuguese Oncology Institute of Porto (IPO Porto), Porto, Portugal
3 Department of Medical Oncology, Portuguese Oncology Institute of Porto, Portugal
4 Department of Pathology, Portuguese Oncology Institute of Porto, Porto, Portugal
5 Department of Pathology and Molecular Immunology, Institute of Biomedical Sciences Abel Salazar – University of Porto (ICBAS-UP), Porto, Portugal
E-mail address: silvana_lobo_sousa@live.com.pt (S. Lobo)

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. Around 70% of all BrC are hormone-receptor positive, that is the major part of breast tumors is luminal-like. H3K27m3 is a gene repression marker and is associated with gene silencing, playing a crucial role in cell proliferation and differentiation. H3K27me3 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.

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 H3K27me3 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).

References