

of high cytoplasmic AR expression in tumour cells and CD3 T-cells predicts poor outcome for patients diagnosed with PCa.

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ALDHs as potential biomarkers in myeloid neoplasms – Preliminary study

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Aim: The aim of the study is to evaluate the expression of aldehyde dehydrogenase (ALDH) in patients with myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML) to verify their potential as a marker for the diagnosis and/or prognosis of these diseases.

Introduction: ALDH superfamily is a group of 19 enzymes critical to the protection against toxic aldehydes, and have been associated with multiple diseases, namely in cancer. MDS are characterized by ineffective hematopoiesis associated with progressive peripheral blood cytopenias, and a predisposition toward leukemic transformation. MDS pathophysiology is a complex multistep process that involves genetic and epigenetic abnormalities in genes associated with differentiation, cellular proliferation, and apoptosis. Since ALDHs are involved in some of these biological processes, the deregulation of these enzymes may influence MDS and AML development.

Methods: To this end, we analyzed the expression levels of 8 ALDH isoforms, ALDH1A1, ALDH1A2, ALDH1B1, ALDH1L1, ALDH1L2, ALDH3A2, ALDH4A1, and ALDH16A1, in 31 patients (16 MDS and 15 LMA) and 19 healthy controls. ALDH expression levels were analyzed using RT-PCR and differentially expressed genes were quantified by qPCR. The statistical analysis was carried out by variance analysis and χ^2 test. Survival were analyzed by Kaplan Meier curves ($p < 0.05$).

Results: Preliminary results indicate that all MDS patients express ALDH16A1 isoform whereas only 67% of controls ($p < 0.05$) show expression of this isoform. Moreover, AML patients have lower ALDH1A2 expression levels than MDS and controls and only 20% of AML patients express this isoform (MDS=54% and controls=55%). The ALDH1L2 is only expressed in chronic myelomonocytic leukemia subtype of MDS. Furthermore, the expression of ALDH isoforms does not appear to influence patient overall survival.

Conclusion: According to these results, ALDH isoforms have differential expression patterns in MDS and AML patients when compared with controls and each other. Further studies are needed to prove their potential as a diagnostic/prognostic biomarkers.

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PS155

Discovery of novel mechanisms of centrosome amplification and their therapeutic value in cancer



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Aim: To understand the mechanisms of centrosome amplification and their therapeutic value in cancer.

Introduction: Centrosomes are the major microtubule-organising centres of animal cells. Centrosome amplification (CA) – the presence of more than two centrosomes in a cell – is a common feature in cancer¹ and was recently shown to be sufficient to drive tumorigenesis.² Recent work from the Bettencourt-Dias Lab has identified a new recurrent feature of cancer cells: centriole over-elongation, which also promotes CA. However, origins of those abnormalities and their therapeutic value remain poorly understood.

Methods: We have screened the NCI-60 panel of human cancer cell lines³ for centriole number and individual length to test their frequency and interdependence. We have thereby also generated a metric capturing each abnormality level per cell line that we then correlated with the publicly available molecular (e.g. genomic, transcriptomic and proteomic) and drug-sensitivity quantitative profiles for that panel.

Results: Our single-centriole analyses showed that longer centrioles are more common in cells with CA and that cells do not control their overall centriolar mass when the centriole number increases. Moreover, cancer cell lines with longer centrioles proliferate slower due to an accumulation of cells in G1 phase, suggesting that centriole length defects could lead to a cell cycle delay in G1. In addition, our original genome-wide approach highlighted putative mechanisms associated with susceptibility to both abnormalities, such as the proteasome protecting cells from CA. Correlation with drug activity identified some compounds as potential therapeutic options to selectively target cells with higher incidence of centriole abnormalities.

Conclusion: This work provides the first single-centriole-level portrait of centriole abnormalities in cancer and contributes to the understanding of their molecular origins, namely by revealing novel molecular mechanisms in cell cycle biology. Given the cancer-specificity of these abnormalities, the identified compounds will inspire the development of drugs to selectively target cancer cells.

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References

- Chan JY. A clinical overview of centrosome amplification in human cancers. *Int J Biol Sci.* 2011;7:1122–44.
- Levine MS, et al. Centrosome amplification is sufficient to promote spontaneous tumorigenesis in mammals. *Dev Cell.* 2017;40:1–10.
- Shoemaker RH. The NCI60 human tumour cell line anticancer drug screen. *Nat Rev Cancer.* 2006;6:813–23.

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