



ANALYSIS OF DIAGNOSTICALLY RELEVANT DNA METHYLATION MARKER REGIONS IN CERVICAL CANCER AND ITS PRECANCEROUS LESIONS USING NEXT GENERATION SEQUENCING*

Presenter: Carolin Dippmann
Pharma-Biotechnologist
oncgnostics GmbH

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Objectives

DNA methylation, as an epigenetic mechanism, is an early event in cervical carcinogenesis. In several studies, indications were found that the degree of methylation of marker regions may correlate with the severity of the lesion.

The objective of this work is to explicitly assign the methylation of diagnostically important marker regions to tumour cells. Furthermore, the methylation level of these marker regions is investigated in relation to the severity of the lesion.

Methods

DNA recovered from manually microdissected fresh-frozen CIN and cancer tissue (CIN/tumour as well as stroma regions) was bisulfite-treated and subjected to a subsequent bisulfite-specific PCR. PCR amplicons obtained for the marker regions ASTN1, DLX1, ITGA4, RXFP3, SOX17, ZNF671, FAM19A4, mir124-2 and POU4F3 were sequenced for each sample on an IonTorrent PGM using the Ion 318 Chip Kit. The reads were mapped against the human reference genome hg38.

In total, 56 samples from 41 patients are being examined. The samples were histologically defined as 6 CIN1, 9 CIN2, 16 CIN3 and 25 cervical cancer samples.

Results

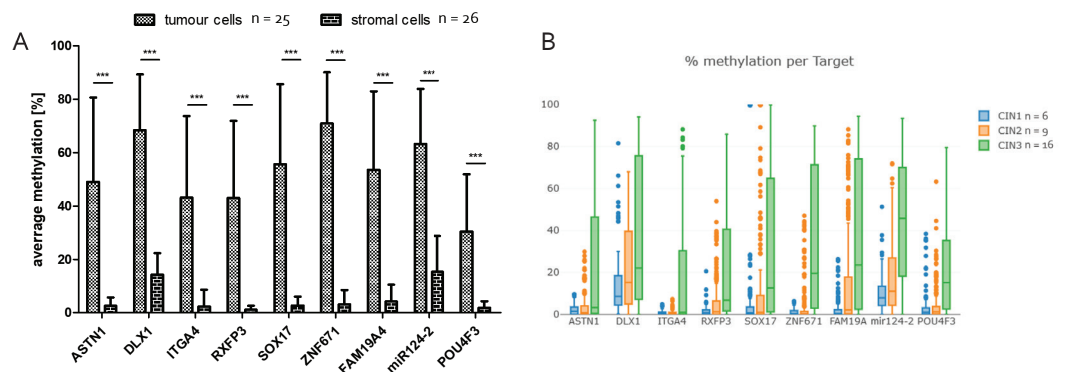
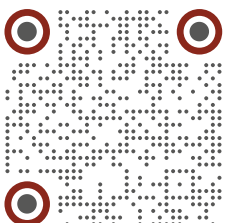


Figure A: Average methylation level of diagnostically relevant DNA marker regions

Figure B: Average methylation level of precancerous lesions

oncgnostics GmbH
Winzerlaer Str.2
07745 Jena | Germany
+49 3641 5548500

kontakt@oncgnostics.com
www.oncgnostics.com



Conclusion

In general, the average methylation is higher than 40% for tumour cells and lower than five percent for stromal cells. Due to the significant difference in the methylation level between tumour and stromal cells, a clear assignment of methylation to the tumour regions can be made. In a first overview it seems that the methylation of the markers increases with the severity of the lesion.

*Carolin Dippmann¹, Martina Schmitz¹, Alfred Hansel¹, Julie Krainer², Klemens Vierlinger², Lars Jansen³, Matthias Dürst³

¹oncgnostics GmbH, Jena, Germany

²Austrian Institute of Technology GmbH, Vienna, Austria

³Department of Gynecology, Jena University Hospital, Jena, Germany