COMPARISON OF mRNA EXPRESSION PATTERN OF RETINOID AND RETINOID X NUCLEAR RECEPTOR SUBTYPES IN THYROID CARCINOMAS, BREAST CANCER AND RENAL CARCINOMAS

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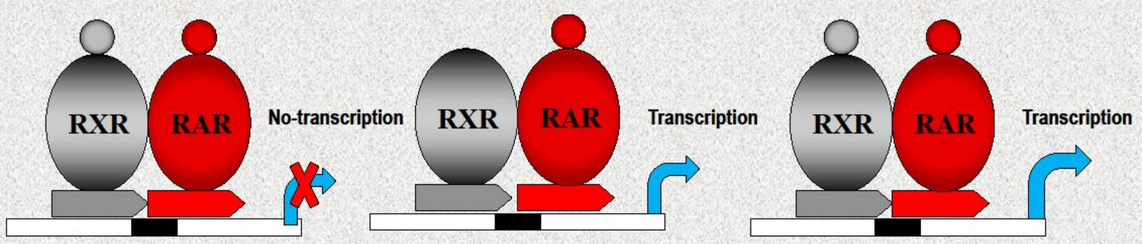
INTRODUCTION

Nuclear retinoid receptors (RARs) upon a ligand binding act as all-*trans* retinoic acid-inducible transcription factors interacting as heterodimers with nuclear retinoid X (rexinoid) receptors (RXRs). The disruption of retinoic acid (RA) signalling pathways is believed to underlie the etiology of a number of malignancies. Retinoids - cell differentiation agents that may "reprogram" tumours, i.e. retinoic acid derivatives or retinoic acid related compounds with reduced teratogenic and other side effects are still highly required.

Conditional heterodimers

RXR/RAR



They are unresponsive to rexinoids, but these (RXR) agonists superactivate transcription by synergizing with RAR agonists.

AIM OF THE STUDY

In this study, we have investigated expression pattern of retinoid receptor subtypes (RARalpha, RARbeta, RARgamma) and rexinoid nuclear receptor subtypes (RXRalpha, RXRbeta, RXRgamma) in three different organ malignancies, i) thyroid different carcinoma tissues, ii) breast cancer, and iii) renal cancer tissues.

MATERIALS AND METHODS

Determination of mRNA Levels Encoding Selected Retinoid/Retinoid X Nuclear Receptors and Nuclear Receptor Coregulators. Total RNA was isolated using Trizol reagent according to the manufacturer's instructions. Concentration of RNA was quantified by spectrometry at 260 nm and purity was assessed from the ratio of absorbances A_{260nm}/A_{280nm}. Reverse transcription (RT) was performed with 2 µg of total RNA and the Ready-to-Go You-Prime First-Strand Beads (Amersham Pharmacia Biotech Inc., USA) according to the manufacturer's protocol. PCR was performed in a 25 µl total volume consisting of 4 µl RT mixture, 1x PCR buffer, 1.5 mmol/l $MgCl_2$, 0.2 mmol/l dNTP, 1 pmol of each specific gene primer set and 0.3 U of DyNAzyme II DNA polymerase (Finnzymes OY, Finland) in buffer provided by the manufacturer. The PCR products were separated on 2 % agarose gel and stained with ethidium bromide. The band intensities were measured using the STS 6220I Documentation System (Ultralum, USA) and normalized to the band intensity of PCR product corresponding to the GAPDH house keeper gene .

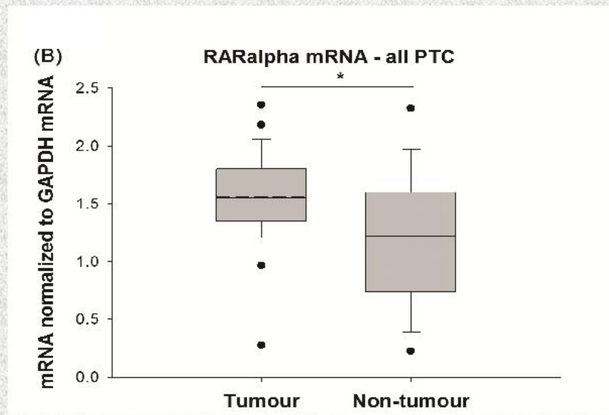
RESULTS

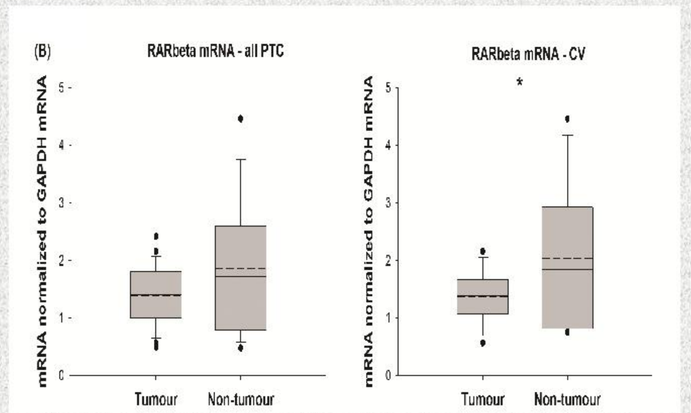
Significantly increased expression of RARalpha and RARgamma in overall group of papillary carcinoma patients was demonstrated. In breast cancer, the expression of respective RAR subtypes was in the following order: RARalpha > RARbeta > RARgamma. Among RXR subtypes, only RXRgamma was markedly diminished in breast cancer tissue. In renal carcinomas, expression of RARalpha and RARbeta was higher when compared to intact kidney tissue. Expression of RARgamma was found to be markedly decreased in all renal tumours. All renal tumours were capable to express RXRalpha and RXRbeta. Expression of RXRgamma was markedly lower in comparison with intact renal tissue.

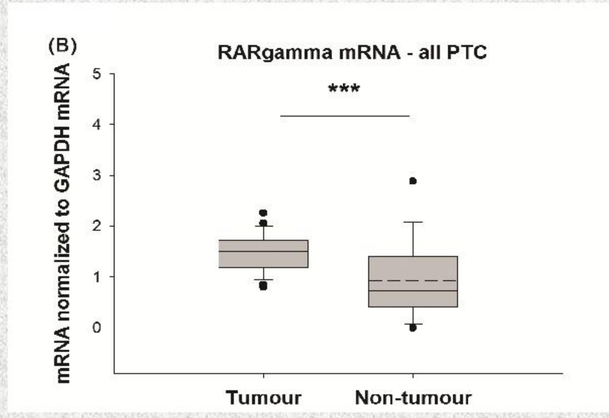
CONCLUSION

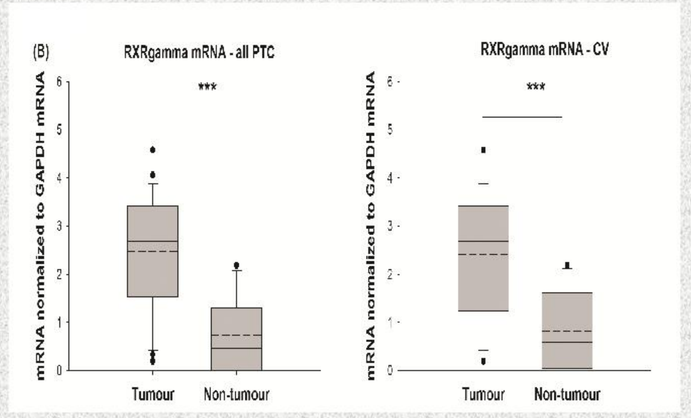
The molecular mechanisms demonstrating differences in RAR and RXR subtype mRNA expression patterns in thyroid carcinomas, breast and renal cancer may find exploitation in clinical oncology, predominantly, in the differential diagnosis of different organ neoplasms.

Thyroid papillary carcinoma

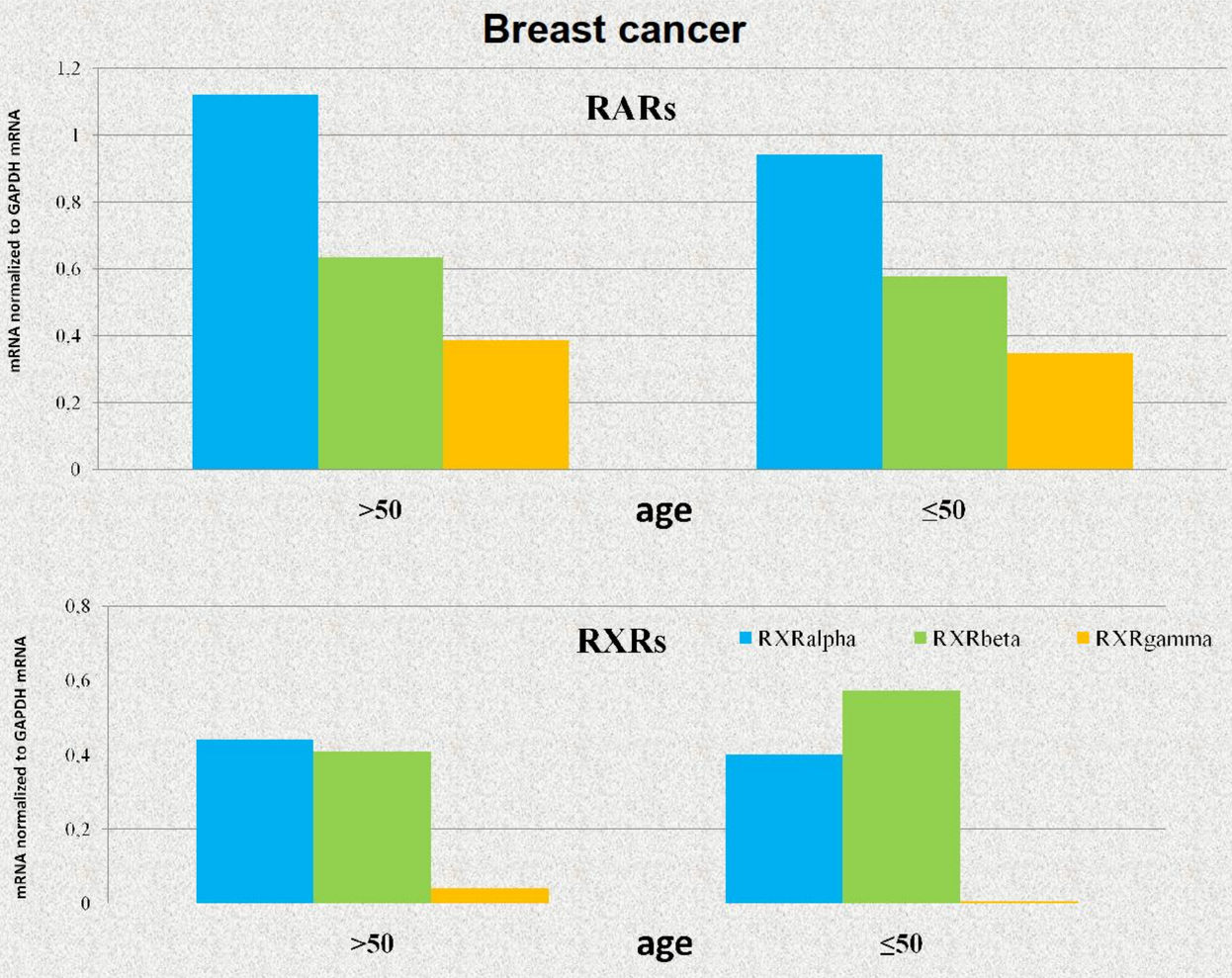




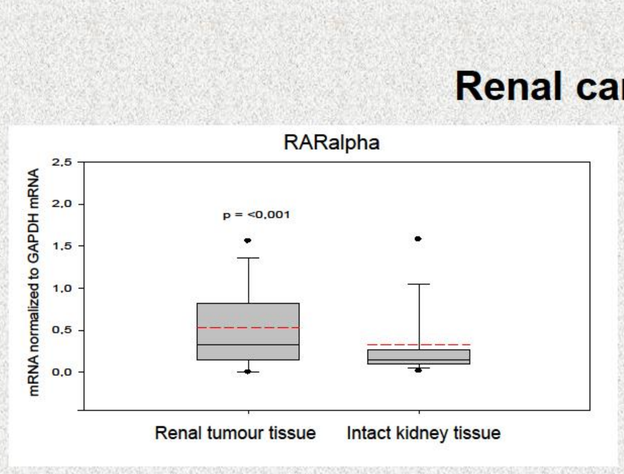


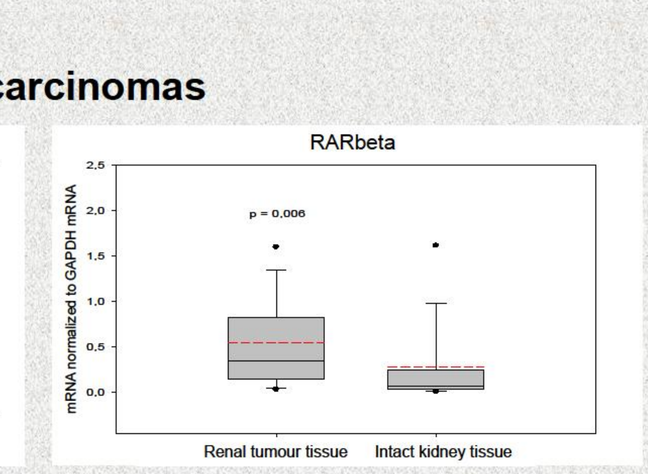


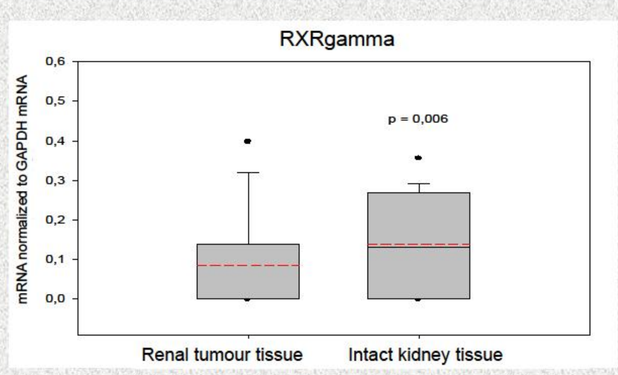
Breast cancer

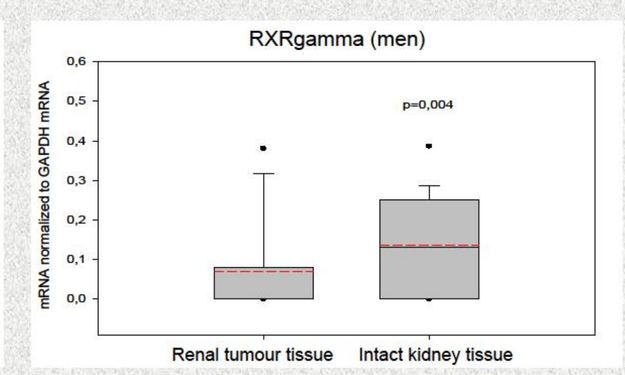


Renal carcinomas









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