Program Number 109

Cell Biology Friday Poster Basic

MCT8 EXPRESSION IS DEVELOPMENTALLY REGULATED IN THE RODENT LUNG

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The lung is a target tissue of thyroid hormone (TH). Triiodothyronine (T3) regulates expression of alveolar epithelial cell sodium pumps, thus controlling lung fluid clearance (American J of Physiology 285(3):L762). Further, lung thyroxine (T4) influx is saturable at low hormone concentrations, suggesting a carrier-mediated transport process (Microvascular Research 37:188). Currently, little is known about TH transporters expression in the lung, the regulation of their transcription, and the functional significance in this tissue. Therefore, we have begun characterizing the developmental and thyroidal expression profiles of TH transporters expressed in lung. For these studies, lungs were harvested from euthyroid rats at different developmental stages: gestational day 19, postnatal days 1 (P1), 10, and 60. Further, lungs were harvested from P60 rats of different thyroidal status: Euthyroid control groups, methimazole-treated (hypothyroid), and T4-treated (hyperthyroid) rats. Total lung RNA was isolated and quantitative real-time RT-PCR was performed against monocarboxylate transporter 8 (MCT8) and organic anion transport protein (Oatp1c1) mRNAs. We determined that MCT8 is expressed in lung throughout development, while Oatp1c1 expression was not detected at any developmental age. MCT8 mRNA levels were highest during late lung development (i.e., gestational through P1), then rapidly declined by P10. This reduction in expression represents a 3-fold decline in relative MCT8 mRNA levels. Assessment of MCT8 in adult euthyroid, hyperthyroid, and hypothyroid lungs yielded no change in expression. Our data suggest MCT8 are developmental, but not regulated by thyroidal status in rodent lung. This early expression of MTC8 may play a perinatal role in clearing lung fluid via alveolar epithelial cell sodium pumps. Other TH transporters may predominate in the mature lung, and/or be regulated by thyroidal state. We are currently examining the expression patterns of other TH transporters including: Oatp1a4, Oatp1a5, Oatp1b3, Oatp4a1, Oatp4c1 and LAT1. These results will be shared at the ATA Conference.

Program Number 110

Iodine Uptake and Metabolism Friday Poster Basic

IODINE ALTERS GENE EXPRESSION PROFILE IN THE MCF-7 BREAST CANCER CELL LINE

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Background: Significant data exists demonstrating that iodine has an inhibitory effect on breast cancer growth, likely through inhibition of cancer promotion. Although both human and animal studies have verified the importance of iodine on the maintenance of healthy breast tissue, little is known about the molecular pathways involved. Evidence suggests that iodine's effect be partially mediated through interactions with the estrogen receptor pathway. *Procedure:* MCF-7 cells (an estrogen receptor positive breast cancer cell line) were grown to 70 percent confluence under standard ATCC condition. Cells were treated with medium containing all-trans-retinoic acid (tRA) for 24 hours to induce the expression of Sodium-Iodide Symporter. Three treatment conditions were then used including 1) standard medium containing tRA only, 2) standard medium containing tRA and estrogen (E), and 3) standard medium containing tRA, E, and Lugol's solution to a concentration of 1 mmol iodine. After 48 hours, mRNA was harvested from the three experimental groups. Microarrays were performed in triplicate between groups 2 and 3 above. Select genes of interest identified through microarray analysis were then verified using quantitative RT-PCR between all three experimental groups. *Results:* 5643 genes overlapped between at least 2 of the 3-arrays, of which 46 showed a greater then 2-fold change (29 up, 17 down) in response to iodine treatment. Quantitative RT-PCR confirmed the results for select genes. Analysis of the 46 genes showed many to be involved in differentiation, cell cycle, hormone metabolism, and cancer growth. *Discussion:* This study provides the first report of the altered gene expression profile which results from iodine treatment of a breast cancer cell line. Several biological pathways involved in cancer growth and development were identified. These changes are possibly responsible for iodine's inhibition of breast cancer promotion.

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Iodine Uptake and Metabolism Friday Poster Basic

EFFECT OF SYSTEMIC TREATMENT WITH RETINOIC ACID AND DEXAMETHASONE ON FUNCTIONAL SODIUM IODIDE SYMPORTER EXPRESSION IN MOUSE BREAST CANCER XENOGRAFTS

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The sodium iodide symporter (NIS) mediates the iodide uptake in the thyroid gland as well as lactating breast tissue, and has been shown to be expressed in the majority of breast cancers. Recently, we and others have reported significant stimulation of all-trans retinoic acid (atRA) induced NIS expression in the estrogen-receptor positive human breast cancer cell line MCF-7 by dexamethasone (Dex), resulting in an enhanced therapeutic effect of ^{131}-I in vitro. In the current study, we therefore examined the in vivo efficacy of Dex stimulation of atRA-induced NIS expression in MCF-7 xenotransplants in athymic nude mice. After systemic treatment with atRA alone or in combination with Dex, iodide accumulation in the tumors was assessed by gamma camera imaging or gamma counteranalysis. Using gamma camera imaging no iodide accumulation was detected in tumors of untreated mice or