Adenosine A2A Receptor: A Prognosis Marker For Lung Cancer

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Technology description

Adenosine A2A receptor expression is increased in lung tumor samples at different stages: (A) Human lung cancer expression panels (I and IV) containing reverse-transcribed cDNA from the different tumor stages were probed with real-time Taqman primers and probes for adenosine A2A receptor and CD31. The A2A expression data were normalized to CD31 expression. The different tumor stages were grouped together and plotted after log transformation. Statistical difference from the normal lung tissue using a 2-sample t test. (B) Normalized A2A expression data were plotted against the different stages of tumors. ANOVA was used to compare the groups, followed by pairwise comparisons of normal tissue versus each of the other groups using Dunnett's procedure. Statistically different from the normal lung tissue. (C) CC1-CC4 show significant positive CD31 (PECAM-1; pinkish-red) immunostaining in the bronchovascular bundles (CC1-CC3) and parenchyma (CC3 and CC4) of normal (atelectatic) lung tissue obtained at surgery. Staining of venous and/or lymphatic vessel endothelium (CC1, arrow) and arterial vessel endothelium (CC2 and CC3, arrowheads) was variable but notably positive, as was the capillary endothelium (CC3 and CC4). Immunostaining for adenosine receptor A2A (brown) was largely absent from these tissues. By contrast, lung cancer specimens from both of these patients (CT1, CT2, CT3, and CT4) stained markedly positive, especially in the tumor stroma. In these regions, CD31-positive-staining cells, likely endothelial cells and/or tumor macrophages, coimmunostained positively for adenosine receptor A2A or, in some cases, A2A-positive cells were immediately adjacent to those staining positively for CD31 (Magnification: 40X). Our scientists have found that: Hypoxia increases ADORA2A in vitro HIF-2alpha and not HIF-1alpha regulates ADORA2A expression Overexpression of ADORA2A or its activation through agonists leads to an increase in endothelial cell proliferation, migration, and branching ADORA2A expression increases in later stage tumor samples collected from lung cancer patients

The role of angiogenesis in tumor survival and metastasis is now well recognized. Hypoxia-inducible transcription factors HIF-1alpha and HIF-2alpha are both known to induce angiogenesis by upregulating a common set of cytokines, including VEGF, but only the activation of HIF-2alpha has been associated with poor prognosis in lung cancer. However, since HIF-2alpha is highly labile, it is a poor candidate for a biomarker. Scientists at National Jewish Health have discovered that the receptor Adenosine A2A (ADORA2A) is expressed only in response to HIF-2alpha activation and more importantly that the expression of ADORA2A is increased in later stage lung tumors. This receptor

could therefore be used as a prognosis marker for lung cancer as well as a potential new target for an anti-angiogenic approach to treating lung cancer.

Application area

A biomarker for HIF-2alpha activation and therefore for poor prognosis in lung cancer. A target for anti-angiogenic therapy in lung cancer

Advantages

Since HIF-2alpha is too labile to be used as a marker, ADORA2A instead can be used as readout of HIF-2alpha activation and can be easily measured at the RNA level in biopsy samples.

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