THE BIOENERGETIC SIGNATURE OF CANCER: BEC INDEX: FB-2007

Description

The evaluation of the energetic metabolism proteins expression as cancer progression molecular markers makes possible to get a BEC index. It is diminished in tumoural biopsies compared to healthy biopsies, getting a higher BEC index reduction in those biopsies with worst prognosis.

The alteration of the mitochondrial energetic function is intimately linked with the malign transformation and progression of cancer, so BEC index can give a new view with a high potential in diagnosis and prognosis of the illness.

Relative expression of the β-F1-ATPasa catalytic subunit, Hsp 60 mitochondrial marker and glucolitic markers: GAPDH and Pyruvate Kinase, are very sensitive metabolic markers (more than 97%). In addition, they are supposed to be good generic markers for tumoural progression in different neoplasies.

Indications

Colon, breast and lung cancer diagnosis and prognosis.

BEC index can determine if the metastasis origin is a primary breast or lung tumour; in addition, it has proved value as a predictive rate to the response against the chemotherapeutic agent 5FU.

Format and technique

Kit with 4 Mab (Monoclonal Antibodies) that let quantify the protein expression through Slot Blot, getting a quantitative data of BEC index. It could also be measured with non quantitative techniques like Immuno-histochemistry or Western Blot.

Observational Study

Breast cancer

101 biopsies from breast tumours, compared to 13 controls, have shown the alteration in the bioenergetic signature as a phenotypic characteristic affecting to more than 97% of the cases.

Studied markers allow to estimate the patients' free-disease survival. Specifically, the β-F1-ATPasa expression allows to identify a subgroup of patients with the worst prognosis (2, 5).

Lung cancer

A) The expression of markers β-F1, Hsp60 and GAPDH in a sample of 90 lung adenocarcinomas, compared to 10 controls, has been studied by two-dimensional gel electrophoresis. Bioenergetic signature is altered in the 97% of the studied patients.

In addition, studied molecular markers allow to discriminate patients with the worst prognosis in the early stages of the illness (2).

B) The expression of markers β-F1, Hsp60, GAPDH and PK has been studied in a sample of 101 lung adenocarcinomas, in "tissue microarray format". The alteration of the bioenergetic signature has been confirmed in a different sample and using immunohistochemistry (3, 7).

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Colon cancer

The expression levels of β-F1, Hsp60 and GAPDH markers have been studied in a sample of 104 colon carcinomas in a "tissue microarray format". The alteration of bioenergetic signature is a general phenotypic characteristic in colorectal cancer and the studied molecular markers let discriminate worst prognosis patients in early stages of the illness (1, 4).

Publications

1. Cuezva et al., (2002). **"The bioenergetic signature of cancer: a marker of tumor progression"**. Cancer Research 62, 6674-6681.

2. Isidoro A. et al. (2004). **"Alteration of the bioenergetic phenotype of mitochondria is a hallmark of breast, gastric, lung and oesophageal cancer"**. Biochem J. 378, 17-20.

3. Cuezva et al. (2004). **"The bioenergetic signature of lung adenocarcinomas is a molecular marker of cancer diagnosis and prognosis".** Carcinogenesis 25, 1157-1163.

4. Young-Kyoung Shin et al (2005). **"Down-regulation of Mitochondrial F1F0-ATP Synthase in Human Colon Cancer Cells with induced 5- Fluorouracil Resistance".** Cancer Research 65, 3162-3170.

5. Isidoro A. et al. (2005). "**Breast carcinomas fulfil the Warburg's hypothesis and provide metabolic markers of cancer prognosis".** Carcinogenesis 26, 2095-2104.

6. Santamaría et al., (2006) **"Efficient execution of cell death in non-glycolytic cells requires the generation of ROS controlled by the activity of the H+-ATP synthase"** Carcinogenesis 27, 925-935.

7. López-Ríos et al. (2007) **"Loss of the mitochondrial bioenergetic capacity underlies the glucose avidity of carcinomas"**. Cancer Research 67.

Intellectual property

- Spanish Patent granted: 200201190 (Priority date: 24th May 2002).

- European Patent granted: 3727509.6, validation granted in Germany, France, Netherlands, Italy, UK, Sweden, and Switzerland.

- PCT National Phase granted in Canada and Japan and in USA.