----- Original Message -----
From: Sergio Stagnaro
To: staff@the-jci.org
Sent: Saturday, April 05, 2014 10:47 AM
Subject: E-Response cancelled?

Sirs,
JCI;

distressingly, the following e-respose cannot yet be found. What accounts for the reason?

Sincerely

Sergio Stagnaro MD
www.sisbq.org
www.semeioticabiofisica.it

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??Articl
???Jean-Pierre David, Denis Mehic, Latifa Bakiri, Arndt F. Schilling, Vice Mandic, Matthias Priemel, Maria Helena Idarraga, Markus O. Reschke, Oskar Hoffmann, Michael Amling, and Erwin F. Wage
???Essential role of RSK2 in c-Fos–dependent osteosarcoma developme???J. Clin. Invest. 2005; 115: 664-6???[Abstra????[Full te? **???eLetter???Submit a respo??? to this arti**
???Letters to the Editor receiv
???A paramount Bias in the Resear?
???Sergio Stagnaro (29 March 205
???http://www.jci.org/cgi/eletters/115/3/6
???A paramount Bias in the Resear ??????29 March 2005
???Sergio Stagnaro, Specialist in Blood, Gastrointestinal, and Metabolic Diseases. Researcher in Biophysical Semeiotic*???Via Erasmo Piaggio 23/8 16037 Riva Trigoso (Genova) It*?
?
???Send letter to journa
???Re: A paramount Bias in the Resear
???Em
Sergio Stagnaro

Sirs,
I think that because congenital functional acidosic mitochondrial cytopathology is overlooked--a "conditio sine qua non" of the most frequent and dangerous human disorders, including osteoporosis and malignancies--this research is fundamentally biased. That is, it does not consider the existence or assess the seriousness as well as the location of Congenital Acidosic Enzyme-Metabolic Histangiopathy, conditio sine qua non of Oncological Terrain (1-4). In fact, e.g., "The phenotype is associated with decreased expression of Phex, an endopeptidase regulating bone mineralization. This defect is probably not mediated by RSK2- dependent phosphorylation of c-Fos on serine 362 in the C-terminus", autors say, and continue "However, in the absence of RSK2, c-Fos–dependent osteosarcoma formation is impaired. The lack of c-Fos phosphorylation leads to reduced c-Fos protein levels, which are thought to be responsible for decreased proliferation and increased apoptosis of transformed osteoblasts". However, malignancy can occur exclusively in individuals involved by Oncological Terrain! In addition, for instance, both environmental risk factors and every drug, including vitamin K in newborn infants, suggested as a risk factor for leukaemia in children, "could" influence some human biological functions and/or bring about

different disorders, such as cancers, exclusively in relation to both the presence and intensity of CAEMH in a well-defined biological system. Apart from the well- known negative influence of oral contraceptive use on breast oncogenesis (3,4) and/or arterial disorders we have to consider the importance of the genetic predisposition ("Oncological Terrain",See also www.semeioticabiofisica.it), as far as the onset of a lot of disorders is concerned, including solid as well as liquid malignancies, such as osteosarcoma. At this point, I would emphasise the well-known pathological powerful influence of a lot of substances, as smoking, on tissue oxygen supply to all biological systems (3, 4). This effect varies notoriously in prevalence and intensity among individuals in relation to the above- mentioned congenital functional mitochondrial cytopathology, i.e. Congenital Acidosic Enzyme-Metabolic Histangiopathy (1, 2, 3). Such as "silent" and dangerous action is easy to evaluate at the bed-side with the aid of a stethoscope. I suggest first investigating (i.e., before whatever research) the presence and intensity of CAEMH in the "tested" population, and soon thereafter assessing prevalence and intensity of the "Oncological Terrain", which always develops on the basis of the above-mentioned congenital cytopathology, and finally the "oncological "real risk" in a well-defined biologica system (1-4). In fact, without this characteristic alteration of psycho-neuro-endocrine-immunological system, associated to "oncological "real risk", oncogenesis is not possible. As a consequence, the importance of the above-mentioned congenital factor should not be overlooked, particularly when we assess a "possible" role in oncogenesis, eg., of whatever growth factor.

1) Stagnaro S., Stagnaro-Neri M. Istangiopatia Congenita Acidosica Enzimo Metabolica. Gazz. Med. It.- Arch. Sci. Med. 144, 423, 1985.
2) Stagnaro S., Stagnaro-Neri M. Una patologia mitocondriale ignorata: la Istangiopatia Congenita Acidosica Enzimo-Metabolica. Gazz. Med. It. - Arch. Sci. Med. 149, 67 1990.
3))Stagnaro Sergio, Stagnaro-Neri Marina. Introduzione alla Semeiotica Biofisica. Il Terreno oncologico". Travel Factory SRL., Roma, 2004.
4) http://www.travelfactory.it/semeiotica_biofisica.htm
5) Stagnaro-Neri M., Stagnaro S., Cancro della mammella: prevenzione primaria e diagnosi precoce con la percussione ascoltata. Gazz. Med. It. – Arch. Sc. Med. 152, 447 1993
6) Stagnaro-Neri M., Stagnaro S., Diagnosi Clinica Precoce dell'Osteoporosi con la Percussione Ascoltata. Clin.Ter. 137, 21-27, 1991 [Pub-Med indexed for MEDLINE]

Articles:
Jean-Pierre David, Denis Mehic, Latifa Bakiri, Arndt F. Schilling, Vice Mandic, Matthias Priemel, Maria Helena Idarraga, Markus O. Reschke, Oskar Hoffmann, Michael Amling, and Erwin F. Wagner
Essential role of RSK2 in c-Fos–dependent osteosarcoma development J. Clin. Invest. 2005; 115: 664-672 [Abstract] [Full text] **eLetters: Submit a response to this article**
Letters to the Editor received:
A paramount Bias in the Research.
Sergio Stagnaro (29 March 2005)
http://www.jci.org/cgi/eletters/115/3/664

A paramount Bias in the Research. 29 March 2005

Sergio Stagnaro, Specialist in Blood, Gastrointestinal, and Metabolic Diseases. Researcher in Biophysical Semeiotics. *Via Erasmo Piaggio 23/8 16037 Riva Trigoso (Genova) Italy*

Send letter to journal:

Re: A paramount Bias in the Research.

Email
Sergio Stagnaro

Sirs,
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