Global Science Research Journals

Global Journal of Medicine and Medical Sciences

Open Access

Blood ACE phenotyping: a way to precision medicine

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Abstract

Elevated ACE expression in tissues (which is generally reflected by blood ACE) is associated with increased risk of several cardiovascular diseases. Elevated blood ACE is also a marker for granulomatous diseases. Recently, we developed a new approach for detailed characterization of ACE status in the blood – ACE phenotyping.

Objective and Methodology

We applied ACE phenotyping to characterize blood ACE in 200 serum or citrated plasma of 200 unrelated patients. ACE phenotyping include 1) simultaneous determination of ACE activity with 2 substrates (ZPHL and HHL); 2) calculation of ratio of hydrolysis of two substrates (ZPHL/HHL ratio); 3) determination of the levels of ACE immunoreactive protein and ACE conformation with set of mAbs to ACE.

Principal findings

Only a combination of ACE activity determination with two substrates and determination of the amount of ACE immunoreactive protein with mAb 1G12 allows objectively detect 23 patients (out of 200) with ACE inhibitors in their blood. After excluding such patients we established normal values of ACE in healthy populations – 50-150% from control plasma. Increased of ACE levels more that 150% in 8 patients (out of 200) likely reflects presence of ACE inhibitors (increasing ACE shedding), increase in glycocorticoid or thyroxine production (increasing overall expression of ACE in the body) or systemic sarcoidosis or Gaucher disease. ACE phenotyping also allowed to identify 4 patients with conformationally altered ACE. The screening of unrelated (or healthy) populations for detection of conformationally impaired ACE definitively has clinical significance, because such patients has 2-4 fold of increase in ACE activity with natural substrate Angiotensin 1 (i.e. theoretically having significantly increase local concentration of AII, which is the risk factor for many cardiovascular complications

Conclusions

ACE phenotyping has clinical significance and should be used for patients screening because allows to establish different risk groups based on ACE phenotype.

Biography

Sergei Danilov has completed his/ PhD at the age of 28 years from National Cardiology Center, Moscow, Russia and in 1994 became Doctor of Science (Full Professor Rank) in the same institution. He is the associate professor of University of Illinois at Chicago, USA. He has over 170 publications that have been cited over 5000 times, and his publication H-index is 41. Danilov's laboratory generated over 40 monoclonal antibodies to ACE (angiotensin-converting enzymeand performed full epitope mapping of these mAbs. Actually, Dr. Danilov established new discipline –immunochemistry of ACE and demonstrated enormous diagnostic, research and even therapeutic potential of these mAbs to ACE.

Citation: Sergei M. Danilov, Blood ACE phenotyping: a way to precision medicine, Global Cardiology Congress 2020, 7th International Conference on Cardiology and Cardiovascular Medicine, July 13-14, 2020, Page: 09

Glob. J. Med. Med. Sci. 2020
ISSN: 2449-1888

Volume 8| Issue 4 | 09