Genetic and functional analysis on the role of the novel homologues of angiotensin converting enzyme (ACE) in angiogenesis/blood vessel formation

Fact Sheet

Project Information

ACE IN ANGIOGENESIS

Grant agreement ID: 510029

Project closed

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1 March 2004

End date
28 February 2006

Funded under
Human resources and Mobility in the specific programme for research, technological development and demonstration "Structuring the European Research Area" under the Sixth Framework Programme 2002-2006

Total cost
€ 149 963,00

EU contribution
€ 149 963,00

Coordinated by
INSTITUT OF MOLECULAR BIOTECHNOLOGY OF THE AUSTRIAN ACADEMY OF SCIENCES
Austria

Objective

Inhibition of new blood vessel formation is a promising therapy against cancer, diabetic retinopathy, or rheumatoid arthritis where pathological angiogenesis occurs. However, as shown by the failure of some angiogenesis inhibitors in clinical trials, the m olecular mechanisms of angiogenesis are still elusive and more effective and fine-tuned therapies for angiogenic diseases are awaited. New evidence indicates that angiotensin II, generated by angiotensin converting enzyme (ACE), contributes to the progress ionof diabetic retinopathy and some cancers. The precise role of the renin-angiotensin pathway in angiogensis is unknown. Josef Penninger's laboratory recently identified a novel homologue of ACE, termed ACE-2. In genetic experiments his group showed that ACE2 is a candidate QTL for hypertensions and that loss of ACE2 results in heart failure and decreased heart functions (Crackower et al. Nature 2002). These data provided the first genetic evidence that the renin-angiotensin system has a critical and direc t role in the heart and introduced a novel paradigm for negative regulation of the renin-angiotensin pathway, i.e. ACE2 counterbalances the function of ACE. The goal of this proposal is to identify the role of ACE-family molecules ACE, ACE2, and collectrin and their vasoactive peptide substrates such as angiotensin II in angiogenesis and to develop novel therapeutic strategies to modulate new blood vessel formation in disease. We propose to investigate angiogenesis in knockout mice of ACE, ACE2 and collectr in as well as mice that have mutations in the ACE/ACE2 substrates angiotensinogen, apelin, and bradykinin using murine angiogenesis models. We hypothesize that adult angiogenesis in mammals is conserved in primitive vascular development in fruitfly, since a P-element mutation associated with the Drosophila ACE/ACE2 homologue ACER results in defective heart tube formation. To elucidate yet unknown substrate peptides and/or #'

Fields of science (EuroSciVoc)

medical and health sciences > clinical medicine > **rheumatology**

medical and health sciences > clinical medicine > **oncology**

natural sciences > mathematics > pure mathematics > mathematical analysis > **functional analysis**

medical and health sciences > clinical medicine > ophthalmology > **retinopathy**

medical and health sciences > clinical medicine > **cardiology**

Keywords

Angiogenesis | Angiotensin converting enzyme | Cancer | Fruit Fly | In vivo | Knockout mice | Novel therapeutic targets | Retinopathy | Whole genome screen

Programme(s)

FP6-MOBILITY - Human resources and Mobility in the specific programme for research, technological development and demonstration "Structuring the European Research Area" under the Sixth Framework Programme 2002-2006

Topic(s)

MOBILITY-2.3 - Marie Curie Incoming International Fellowships (IIF)

Call for proposal

FP6-2002-MOBILITY-7
See other projects for this call

Funding Scheme

IIF - Marie Curie actions-Incoming International Fellowships

Coordinator

INSTITUT OF MOLECULAR BIOTECHNOLOGY OF THE AUSTRIAN ACADEMY OF SCIENCES

EU contribution

No data

Total cost

No data

Address

Dr Bohrgasse 3-5
VIENNA
Austria

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