Innovative drugs targeting IDO molecular dynamics in autoimmunity and neoplasia

Dal 2014-02-01 al 2019-01-31, progetto concluso

Dettagli del progetto

<table>
<thead>
<tr>
<th>Costo totale:</th>
<th>Argomento (i):</th>
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<tbody>
<tr>
<td>EUR 2 442 078</td>
<td>ERC-AG-LS7 - ERC Advanced Grant - Diagnostic tools, therapies and public health</td>
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<tr>
<th>Contributo UE:</th>
<th>Invito a presentare proposte:</th>
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<td>EUR 2 442 078</td>
<td>See other projects for this call</td>
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<th>Coordinato in:</th>
<th>Meccanismo di finanziamento:</th>
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<tr>
<td>Italy</td>
<td>ERC-AG - ERC Advanced Grant</td>
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Obiettivo

"Catabolism of amino acids is an ancient survival strategy that also controls immune responses in mammals. Indoleamine 2,3-dioxygenase (IDO), a tryptophan catabolizing enzyme, is recognized as an authentic regulator of immunity in several physiopathologic conditions, including autoimmune diseases, in which it is often defective, and neoplasia, in which it promotes immune unresponsiveness. The PI’s group recently revealed that IDO does not merely degrade tryptophan and produce immunoregulatory kynurenines but also acts as a signal-transducing molecule independently of its enzyme activity. IDO’s signaling function relies on the presence of phosphorylatable motifs in a region (small IDO domain) distant from the catalytic site (large IDO domain). Preliminary data indicate that IDO, depending on microenvironmental conditions, can move among distinct cellular compartments. Thus IDO may be considered a ‘moonlighting’ protein, i.e., an ancestral metabolic molecule that, during evolution, has acquired the DYNAMIC feature of moving intracellularly and switching among distinct functions by changing its conformational state. By means of computational studies, Macchiarulo’s group (team member) has identified distinct conformations of IDO, some of which are associated with optimal catalytic activity of the enzyme whereas others may favor tyrosine phosphorylation of IDO’s small domain. A switch between distinct conformations can be induced by the use of ligands that bind either the catalytic site or an accessory pocket outside the IDO catalytic site. The first aim of DIDO is to decipher the relationships between IDO conformations and multiple functions of the enzyme. A second aim is to identify small molecules with drug-like properties capable of modulating distinct IDO’s molecular conformations in order to either potentiate (a new therapeutic approach in autoimmune diseases) or inhibit (more efficient anti-tumor therapeutic strategy) immunoregulatory signaling ability of IDO."

Informazioni correlate

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<th>Sintesi delle relazioni</th>
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<tr>
<td>Final Report Summary - DIDO (Innovative drugs targeting IDO molecular dynamics in autoimmunity and neoplasia)</td>
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<tr>
<td>Mid-Term Report Summary - DIDO (Innovative drugs targeting IDO molecular dynamics in autoimmunity and neoplasia)</td>
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Ricercatore principale

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Istituzione ospitante

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Beneficiari

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To know more

http://erc.europa.eu/

Argomenti

Healthcare delivery/services - Life Sciences - Medicine and Health

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