High resolution dissection of non-coding determinants of disease

Fact Sheet

Project Information

B-ALLeles

Grant agreement ID: 101061151

DOI
10.3030/101061151

Project closed

EC signature date
8 August 2022

Start date
1 November 2022

End date
31 October 2024

Funded under
Marie Skłodowska-Curie Actions (MSCA)

Total cost
No data

EU contribution
€ 183 600,96

Investment in EU policy priorities

Digital agenda	○	Clean air	○
Artificial Intelligence	○	Climate action	○
Biodiversity	○		

Coordinated by
ST. ANNA KINDERKREBSFORSCHUNG GMBH
Austria

Objective

While mutations at protein-coding sequences have been extensively characterized, the functional role of disease-associated non-coding variants remains largely elusive.

In fact, germline non-coding variants are often associated with increased risk of childhood cancers. In B-cell derived acute lymphoblastic leukemia (B-ALL), the most common type of cancer in children, non-coding sequence variation at lineage-specific genes, such as IKZF1, GATA3 and CEBPE is associated with disease. Interestingly, the strongest risk factor maps at ARID5B, a DNA-binding protein described to promote the removal of repressive histone marks. Still, the role of ARID5B in leukemia and haematopoiesis remains largely uncharacterized. Thus, we hypothesize that non-coding variants associated with B-ALL affect the activity of distal regulatory elements, modulating the expression of ARID5B and other B-cell lineage-specific genes (objective 1). We further postulate that ARID5B promotes the de-repression of lineage-specific genes (objective 2), playing a crucial role in B-cell development and B-ALL initiation and progression (objective 3). To test these hypotheses, I will develop a novel CRISPR screen approach to dissect ARID5B enhancers at single nucleotide resolution (work package 1). I will use a combination of genomics and transcriptomics methods after acute and prolonged degradation of ARID5B to elucidate the molecular function of ARID5B in B-ALL (work package 2). Finally, I will use mouse models and focus on the physiological relevance of ARID5B in B-cell development and leukemia initiation and progression, in vivo. (work package 3). Together, I will dissect the role of non-coding variants at leukemia-associated loci, characterize the molecular function of ARID5B and elucidate the pathophysiological relevance of ARID5B.

Fields of science (EuroSciVoc)

natural sciences > biological sciences > biochemistry > biomolecules > **proteins**

natural sciences > biological sciences > genetics > **mutation**

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

Keywords

non-coding variants | epigenetics | CRISPR screens | hematopoiesis | leukemia | enhancers | GWAS

Programme(s)

HORIZON.1.2 - Marie Skłodowska-Curie Actions (MSCA) MAIN PROGRAMME

Topic(s)

HORIZON-MSCA-2021-PF-01-01 - MSCA Postdoctoral Fellowships 2021

Call for proposal

HORIZON-MSCA-2021-PF-01

See other projects for this call

Funding Scheme

HORIZON-TMA-MSCA-PF-EF - HORIZON TMA MSCA Postdoctoral Fellowships - European Fellowships

Coordinator

ST. ANNA KINDERKREBSFORSCHUNG GMBH

Net EU contribution

€ 183 600,96

Total cost

No data

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Ostösterreich > Wien > Wien

Activity type

Research Organisations

Links

Contact the organisation
Participation in EU R&I programmes
HORIZON collaboration network

Partners (1)

PARTNER

CEMM - FORSCHUNGSZENTRUM FUER MOLEKULARE MEDIZIN GMBH

Austria

Net EU contribution

€ 0,00

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Activity type

Private for-profit entities (excluding Higher or Secondary Education Establishments)

Links

Contact the organisation Website
Participation in EU R&I programmes
HORIZON collaboration network

Total cost

No data

Last update: 15 September 2022

Permalink: https://cordis.europa.eu/project/id/101061151