

PNRR Missione 4, Componente 2, Investimento 1.4 “Potenziamento strutture di ricerca e creazione di "campioni nazionali di R&S" su alcune Key Enabling Technologies”

Iniziativa finanziata dall'Unione europea — NextGenerationEU.

National Center for Gene Therapy and Drugs based on RNA Technology

Sviluppo di terapia genica e farmaci con tecnologia a RNA

Codice progetto MUR: **CN00000041** – CUP UNINA: **E63C22000940007**

Doctorate of National Interest

RNA THERAPEUTICS AND GENE THERAPY

SELECT ONE OF THE FOLLOWING RESEARCH AREA:

- ☒ **Mechanisms of Diseases and Drug Target Identification**
- ☐ **Design and Delivery of New Gene Therapy and RNA-Based Medicines**
- ☐ **Validation and Safety In Preclinical and Clinical Studies**

LOCATION OF THE RESEARCH ACTIVITY (INSTITUTION/DEPARTMENT):

Dept. of Molecular Biotechnology and Health Sciences, University of Torino

[https://www.dbmss.unito.it/do/home.pl/View?doc=Gruppi ricerca/Regenerative Medicine group copy.html](https://www.dbmss.unito.it/do/home.pl/View?doc=Gruppi_ricerca/Regenerative_Medicine_group_copy.html)

TUTOR: Benedetta Bussolati, MD PhD

PROPOSED RESEARCH ACTIVITIES:

Role of RidA proteins in cachexia and tumor metabolism

The Yjg/YEOR057c/UK114 superfamily is a group of ubiquitous proteins, with an interesting common enzymatic property in amino acid metabolism, which leads to their definition of reactive deaminase intermediates (RidA). In particular, the activity of RidA neutralizes the 2-aminoacrylate intermediate metabolite, a highly reactive product capable of inhibiting several metabolic pathways. Cell membrane expression in tumor cells could be related to the defense mechanism of highly proliferating cells against toxic metabolic products accumulating in the interstitium, representing a new and challenging biological observation. On the same way, tumor-released toxic metabolites are known to be implicated in tumor cachexia, a multifactorial disease characterized by body mass loss, negative protein-energy balance and systemic decline. The present project aims to dissect the effect of RidA proteins on tumor cachexia. We will assess both the tumor-related RidA activity and its role in tumor metabolism, as well as the possible detoxifying effects of a systemic RidA activity on circulating tumor catabolites. This will be dissected using in vitro and in vivo models of cachexia. Drugs to modulate RidA metabolic activity will be developed and tested with the final goal to target tumor metabolism, systemic toxin release and inflammation.