MVI-4 | Overcoming immune checkpoint inhibitor resistance by combining checkpoint blockade with innate immune activation

Host unit	Main supervisor	Co-supervisor
Institute of Microbiology and Virology (MVI) Explore the host institute Immunology & Cancer group	Prof. Dace Pjanova View research profile Visit the research group	Dr Zaiga Nora-Krūkle View research profile

APPLICANT FREEDOM The topic defines a research area, not a pre-written project. Applicants may propose a distinct, original approach provided that it remains scientifically aligned with the theme and demonstrably feasible in the host environment.

Research context and rationale

Checkpoint inhibitors targeting the PD-1/PD-L1 axis have transformed cancer treatment, but durable responses remain limited. This research area explores whether combining checkpoint blockade with innate immune activation can enhance antitumour immunity, using melanoma-related experimental systems.

Indicative scientific scope

Projects may evaluate rational combinations of checkpoint inhibition and innate immune activation, including approaches involving double-stranded RNA, provided the candidate defines a testable mechanism, appropriate comparators and a staged validation strategy.

Examples of research questions

- Which innate immune pathways can enhance or restore response to checkpoint blockade in the selected model?
- How does combination treatment affect immune-cell recruitment, activation and cytotoxicity?
- Which tumour or immune features mediate sensitivity, resistance or toxicity-related signals?
- Do in vitro effects translate to physiologically relevant in vivo models under approved conditions?

Possible approaches

- Tumour-immune co-cultures and functional cellular assays.
- Flow cytometry, molecular profiling and microscopy to assess immune dynamics.
- Perturbation of innate immune pathways and evaluation of combination effects.
- In vivo melanoma models at an authorised external facility where scientifically necessary and approved.

METHODS NOTE The approaches above are indicative. Applicants should select and justify methods appropriate to their own questions rather than attempt to include every method listed.

Relevant host expertise and resources

Expertise: Tumour immunology, checkpoint biology, innate immune activation, molecular and cell biology, translational oncology and preclinical model design.

- BSL-2 cell-culture rooms, tumour-immune co-culture models, flow cytometry, cell sorting, tissue dissociation, PCR and microscopy.
- RSU sequencing and bioinformatics capabilities where directly relevant.
- External in vivo capability at the National Institute of Research and Innovation, subject to animal ethics, training and capacity.

ACCESS CONDITION Access to the specialised resources listed above is subject to the conditions described in the separate MVI Host Profile and to project-specific arrangements.

Interdisciplinary and intersectoral opportunities

- Experimental immunology, oncology, pharmacology, bioinformatics and preclinical research.
- Clinical context may be provided by oncology collaborators without implying direct patient recruitment or clinical-trial activity.

Potential collaboration and secondment pathways

- Spanish National Research Council, cancer epigenomics, single-cell and multi-omic analysis, flow cytometry and immune-signature interpretation.
- National Institute of Research and Innovation, SPF rodent handling, tumour models, surgery, IVIS imaging and in vivo study design. Dr. Dace Skrastina is a proposed external mentor for the in vivo component; her involvement and the hosting arrangements will be agreed for the individual project.
- SIA APPLY, applied AI, computer vision, predictive modelling and production-oriented digital-health development.

SECONDMENT STATUS
Participation in a mandatory secondment of 6–12 weeks forms part of KEY-RSU.
The final host, duration, objectives and outputs will be agreed for the selected fellow and aligned with the approved KEY-RSU rules and Career Development Plan. The researcher remains employed by RSU throughout the secondment. Additional host organisations may be considered, subject to confirmation of their suitability, compliance with KEY-RSU requirements and any necessary approvals.

Research training and career development

Scientific training opportunities include advanced immune profiling, flow cytometry, bulk and single-cell RNA sequencing, integrative bioinformatics, experimental design and multi-omic data analysis, according to the selected project. These are complemented by programme-level training in project management, scientific writing, grant preparation and communication. Opportunities to mentor undergraduate and master's students and contribute to guest lectures or practical teaching will depend on the researcher's experience and institutional arrangements. Individual training priorities will be agreed through the Career Development Plan.

Applicant background

Relevant background: Applicants should hold a doctoral degree and demonstrate a strong research background in immunology, cancer biology, molecular and cell biology, pharmacology, or a related discipline. Experience with animal models may be beneficial for some project designs. Candidates should demonstrate the ability to develop and conduct independent research and contribute to the understanding of immune mechanisms relevant to cancer and immunotherapy. Assessment will consider the quality, originality, and relevance of the applicant's research contributions, as well as evidence of collaboration, mentoring, supervision, knowledge sharing, and engagement with the wider research community. Experience in immunology, tumour biology, experimental model systems, translational research, drug development, or biomarker studies will be considered an asset where relevant to the proposed project. Expertise in specific methodologies will be evaluated in the context of the proposed research and the applicant's overall competencies, achievements, and potential.

No additional position-specific eligibility requirement should be inferred from this profile unless it is explicitly included in the approved Full Call Text.

Competences that may strengthen the proposal

The following experience may strengthen a proposal but is not an automatic eligibility requirement:

- tumour immunology, immune-checkpoint biology or innate immune activation;
- tumour–immune co-culture systems and functional cellular assays;
- flow cytometry, microscopy or molecular profiling;
- pharmacological or molecular perturbation studies;
- preclinical experimental design and evaluation of combination effects;
- in vivo research, where such work is scientifically necessary and formally approved.

Previous animal-model experience should be treated as relevant only where required by the candidate's proposed design. It must not be converted into a general eligibility condition unless this is explicitly established in the approved call documentation.

Feasibility boundaries

- The proposed research should remain within the scope of preclinical investigation and should not imply clinical testing or patient intervention.
- Any in vivo studies must be scientifically justified, supported by the necessary ethical approvals, and compatible with available facilities, expertise, and resources.
- Claims regarding combination or synergistic treatment effects should be supported by appropriate controls, a clear biological rationale, and robust statistical analysis.
- The project scope should be aligned with the availability of experimental models, infrastructure, and allocated research resources.
- Proposals should include a realistic strategy for validation and reproducibility of key findings.

Ethics, data and responsible research

- Research involving animal models must comply with applicable ethical and regulatory requirements, including prior authorisation, implementation of the 3Rs (Replacement, Reduction and Refinement), and appropriate training of research personnel.
- The use of innate immune agonists, experimental compounds, and other biologically active agents requires appropriate biosafety assessment, risk management procedures, and compliance with laboratory safety regulations.
- Study design, data collection, and analysis should promote research integrity, reproducibility, and transparency through the use of appropriate controls and robust documentation.
- Positive, negative, and inconclusive findings should be reported transparently to support reproducibility and the reliable advancement of scientific knowledge.
- Applicants are expected to adhere to the principles of responsible conduct of research, including data integrity, transparency, and responsible communication of research findings and their limitations.

Expected contribution

The research is expected to generate mechanistic and preclinical evidence on strategies for overcoming checkpoint-inhibitor resistance and to clarify the conditions under which innate immune activation may be beneficial.