

## Oferta de contrato predoctoral para unirse al grupo de Juan Carlos Acosta:

### ¡Únete a la vanguardia de la investigación en cáncer y senescencia celular!

El Grupo de Supresión Tumoral, Senescencia Celular, SASP y Terapias Innovadoras ofrece un contrato predoctoral para realizar la tesis doctoral en el estudio de la **señalización del sistema inmunitario innato** asociada a la **senescencia celular en cáncer de pulmón**.

Trabajarás en un equipo dinámico y multidisciplinar, con un enfoque pionero en la investigación de la **senescencia**, estudiando los **sensores de daño celular** que regulan el **secretoma senescente (SASP)** y que son clave en la activación de la respuesta antitumoral, contribuyendo a identificar **nuevas estrategias terapéuticas** contra el cáncer de pulmón.

**Modalidad:** Ayuda para la formación de personal investigador predoctoral PIF2024 (antiguas FPI).

**Duración:** 4 años de contrato.

**Ubicación:** Instituto de Biomedicina y Biotecnología de Cantabria (IBBTEC)-CSIC, Santander.

**Título del Proyecto:** *Caracterización y Aprovechamiento de Inflamasomas y Pyroptosis en Senescencia Celular y Cáncer* (PID2023-146497OB-I00).

**Investigador Principal:** Dr. Juan Carlos Acosta Cobacho.

**Fecha estimada de incorporación:** Primer trimestre de 2025.

### Requisitos

Buscamos a un graduado con Máster en Biología, Bioquímica, Biomedicina o áreas afines, con interés en biología del cáncer y la senescencia celular. Experiencia previa biología molecular y en modelos animales será valorada positivamente.

Envía tu CV, una **carta de motivación**, y los **datos de contacto de dos referencias** a: [jc.acosta@csic.es](mailto:jc.acosta@csic.es)

Información del grupo: <https://web.unican.es/ibbtec/en-us/about-ibbtec/team/members/member-detail?d=JuanCarlosAcostaLAB>

### Descripción del proyecto

La senescencia celular inducida por el estrés oncogénico es un mecanismo clave que impide la proliferación de células mutadas y frena el desarrollo y la progresión tumoral. Las células senescentes además, presentan un fenotipo secretor asociado, lo que se conoce como el SASP, que es un complejo programa proinflamatorio que modula los efectos en el microambiente y el sistema inmunitario. En nuestro laboratorio, hemos identificado que los sensores del sistema inmunitario innato como TLR2, cGAS-STING y el inflamasoma, detectan moléculas que son producidas en situaciones de estrés y daño celular, lo que señala para la activación del arresto celular, el desarrollo del SASP, y la respuesta supresora de tumores. El objetivo último de este proyecto es descubrir y caracterizar nuevos componentes de estas vías inmunitarias en cáncer de pulmón, investigando su papel en modelos celulares de senescencia, en pacientes de cáncer de pulmón, y en modelos animales. Caracterizaremos el mecanismo de funcionamiento de estas vías de detección de daño celular en senescencia, e investigaremos en modelos de ratón de cáncer de pulmón por activación oncogénica de Kras, cuál es su efecto supresor de tumores. Trabajarás en un equipo dinámico y multidisciplinar, con un enfoque pionero en la investigación de la **senescencia celular** como mecanismo supresor de tumores. En este proyecto, estudiaremos los **sensores del sistema inmunitario innato**, como TLR2, cGAS-STING e inflamasomas, que son reguladores clave en la activación inflamatoria y la respuesta antitumoral. Con este proyecto estarás contribuyendo a descubrir cómo estos componentes pueden ser utilizados para desarrollar **nuevas estrategias terapéuticas** contra el cáncer de pulmón.

### Publicaciones del grupo en el tema:

El grupo tiene un sólido historial estudiando la senescencia celular y el SASP. El Dr Acosta describió por primera vez el SASP, la senescencia paracrina y el papel del inflamasoma en su regulación (1, 2). Desde entonces, el grupo ha avanzado en la comprensión del papel de los sensores inmunitarios innatos en la senescencia y la supresión tumoral. Los hallazgos clave incluyen el mecanismo en senescencia: de TLR2 en la regulación del SASP y en la supresión tumoral en el carcinoma de pulmón no microcítico, del inflamasoma de caspasa-4 en senescencia por bacterias, de la senescencia inducida por estrés ribosomal, y del complejo de poros nucleares regulando el SASP (3-7). Además, el grupo ha identificado senolíticos mediante IA (8).

1. J. C. Acosta *et al.*, *Cell* **133**, 1006-1018 (2008).
2. J. C. Acosta *et al.*, *Nat Cell Biol* **15**, 978-990 (2013).
3. A. Pantazi *et al.*, *Aging Cell* **18**, e12981 (2019).
4. I. Fernández-Duran *et al.*, *Cell Death Differ* **29**, 1267-1282 (2022).
5. F. R. Millar *et al.*, *T Cell Rep* **41**, 111596 (2022).
6. M. Barradas *et al.*, *Genes Dev* **23**, 1177-1182 (2009).
7. P. Hari *et al.*, *T Sci Adv* **5**, eaaw0254 (2019).
8. V. Smer-Barreto *et al.*, *Nat Commun* **14**, 3445 (2023).

**Additional information:****Training program:**

The student will enrol in the 'Biología Molecular y Biomedicina' PhD Program at the University of Cantabria, which adheres to the regulations for PhD studies in Spain (Real Decreto 576/2023). Recognized with the 'Mención hacia la Excelencia' award by the Spanish Ministry of Education (ref. MEE2011-0208), the program is an integral part of the 'Escuela de Doctorado de la Universidad de Cantabria' (EDUC), one of the first established under the previous RD99/2011 regulation. The doctoral program is implemented in line with the aforementioned 'Real Decreto' and includes the following new features: a) The program duration extends four years, culminating in the submission of the doctoral thesis. b) Prior to thesis submission, evaluations from two external researchers to the University of Cantabria (UC) are required.

The training plan comprises interdisciplinary courses and routine thesis reviews by an Academic Committee, including two external researchers. Additionally, the postgraduate school conducts an annual review of the student's progress, evaluating and approving the PhD activities and research plan.

PhD students participate in weekly lab meetings, providing opportunities for feedback and scrutiny through interactions with the supervisor and other lab members. Moreover, the IBBTEC offers robust internal seminars led by PhD students and postdocs, as well as a series with distinguished researchers. The students propose, organize and host one invitation yearly from of the seminar program. Furthermore, PhD students are expected to attend at least one national conference annually and participate in international meetings.

A three-month placement in a renowned international laboratory is planned, offering an opportunity for international doctorate recognition. The PI's extensive international network will facilitate the student's placement in a leading institution abroad for their PhD and postdoctoral studies. Significantly, the PI maintains collaborations with eminent groups in the UK and the USA relevant to the project, potentially serving as sites for the PhD placement. These collaborations include partnerships with Wendy Bickmore for advanced super-resolution microscopy and Alex Von Krigsheim for cutting-edge proteomics, both in Edinburgh; Andy Finch for metabolomics at the Barts in London; Stephen Tait for mitochondria and cell death-inflammation at the Beatson Institute; and a robust collaboration with Joao Passos at the Mayo Clinic in Minnesota for animal models of senescence and mitochondria studies.

The PI, with considerable experience teaching the Cancer Biology and Medicine course at the University of Edinburgh, currently serves as a professor in the Molecular and Cellular Biology and Biomedicine PhD program at the University of Cantabria. The PI has a proven track record in PhD supervision, having overseen four PhD theses to successful completion, with three published in top-tier international journals and the fourth nearing submission. The student will be thoroughly integrated into the lab's principal project, 'CALIPYRSC', under the direct supervision of the PI. Training will encompass the group's expertise in molecular and cellular biology techniques, cellular senescence, high-throughput screening, advanced automated high-content microscopy, and cancer animal models. Our lab emphasizes continuous supervision and education in experimental techniques, supported by a solid scientific foundation for each project, facilitated through weekly one-on-one meetings with the PI.

**Human, material and equipment resources available for the execution of the Project.**

Dr Juan Carlos Acosta's laboratory was established at the Cancer Research UK Edinburgh Centre in January 2013, and it is located since September 2021 at the Institute of Biotechnology and Biomedicine of Cantabria (IBBTEC). The IBBTEC is a joint centre between the CSIC (Spanish National Research Council) and the University of Cantabria, constituting a leading infrastructure for research in Biomedicine in the autonomous community of Cantabria, nationally and internationally, with highly prestigious research groups in various fields such as cancer biology, transcription regulation, development, immunology, and microbiology, among others. This creates an ideal environment for the research carried out by the group.

The Acosta group at the IBBTEC operates a 75 m<sup>2</sup> laboratory, fully equipped with the necessary labware for executing the project. The facilities are set with all the necessary equipment to perform all basic molecular and cellular biology techniques required for the project. The building has common facilities for conducting experiments in cellular and molecular biology, cell cultures, transmitted light microscopy, fluorescence, and confocal

microscopy, as well as facilities for working with mouse animal models. The IBBTEC holds an SPF and conventional mouse facility suited to perform all the necessary animal experimentation. Recently, because of the incorporation of Dr Acosta's group, IBBTEC applied for and obtained a funding of 500,000 euros from the EU Resilience Funds to finance the acquisition of an automated microscope for high-content phenotypic screening, which has already been installed at the centre. Dr Acosta's research group has extensive experience in handling and using such screening platforms and in training users of this platform, and will lead the setup, use, and management of this platform at IBBTEC. The high-content screening platform is already in operation and will be of great importance in the research activity of the group and specifically in the development the CALIPYRSC project. The Operetta at the IBBTEC has specific FRET capabilities, critical for the project.

The group is currently composed of PI Juan Carlos Acosta, postdoctoral researcher Dr. Andrea Quintanilla, who is funded with the “Proyecto Generacion de Conocimiento 2022” project, predoctoral researcher Paula Blanco, who is FPU scholar, and contracted researcher seeking for a PhD, Sofía Morán. Dr Quintanilla has been part of the group since its first stage in Edinburgh and moved to IBBTEC from its establishment in Spain. Dr Quintanilla has been an indispensable component of the group from the beginning, and even more so for the transfer of knowledge and experience in establishing the group in Santander. Dr Quintanilla is a co-author on many the group's publications and is the first author of an article recently published in Nature Communications, which describes an Artificial Intelligence-based method to screen chemical molecules, identifying three new senolytic drugs (that cause cell death specifically in senescent cells). In addition, the bulk of Dr. Quintanilla's work during her postdoctoral period in the group, which describes an essential role of lipid metabolism in establishing the transcriptional program of cellular senescence, is in preparation and will soon be submitted for publication. Paula Blanco is a PhD student with an outstanding academic record, leading to her being awarded a predoctoral scholarship from the University of Cantabria and an FPU grant from the Ministry of Science, Innovation and Universities of the Government of Spain. The latest addition to the group is Sofía Morán, a graduate in biotechnology who was a student in the Master's in Biomedicine program at UC, and who has also an outstanding academic record. Attracting talent for the development of projects is critical for the consolidation of the research program at IBBTEC. It is crucial for us to incorporate students into our group through the obtainment of predoctoral grants such as the FPI, to develop and consolidate our competitive research program.