

Activatable Catalytic Metallodrugs in Cancer Research

IMDEA - Nanociencia Institute

www.nanociencia.imdea.org

CENTRE DESCRIPTION

IMDEA Nanociencia is a young interdisciplinary research centre dedicated to the exploration of basic nanoscience and the development of applications of nanotechnology in connection with innovative industries.

Our purpose-built building was inaugurated in 2014 and features state-of-the-art facilities for 21st century science, where the frontiers between fields disappear and Physics, Chemistry, Biology, Engineering, and Medicine merge. It features more than 30 operative laboratories with over € 16 M worth of equipment - including the Centre for Micro and Nanofabrication. We are located at the UAM Campus, with access to all the facilities of one of Spain's largest and most prestigious Universities. The UAM Campus is just a few minutes away from Madrid's lively city centre, connected by "cercanías" trains and several bus lines.

We are over 150 scientists, with different professional and personal backgrounds. Approximately 40% of our PhD and postdocs come from outside Spain, representing every corner of the world, from Germany to China, from the USA to Singapore –a true international environment in which to develop your scientific career. Women make up 36% of our scientific and 62% of our management staff. No matter who you are or where you come from, you will feel welcome from the very first minute.

We take science seriously and value quality over quantity. Our scientists enjoy tackling complex multidisciplinary problems, often within in-house collaborations, so all of our students receive truly interdisciplinary training. We also enjoy publishing in the very best journals, with >200 publications a year, and an institutional h index of 79. Check out our webpage <http://nanociencia.imdea.org/>, facebook @IMDEANanociencia or twitter @IMDEA_Nano for more information.

So if you are a talented, hard-working individual with a real interest in Science, IMDEA Nanociencia is the right place for you! Come work with us!

ADDRESS

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AREA OF KNOWLEDGE

Physical Sciences, Mathematics and Engineering

GROUP OF DISCIPLINES

Chemistry and Chemical Engineering

Physics

GROUP LEADER

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Research Group Website: <http://nanociencia.imdea.org/metallodrugs-to-modulate-cancer-cell-machinery/group-home>

Research project/ Research Group description

Our main goal is to synthesise new metallodrugs with exciting mechanisms of action, primary through (bio)catalysis. The drugs (based on platinum, ruthenium, osmium, iridium, and rhodium) are designed to be activated only at the tumour site. Upon activation, the metal-based compounds exert a lethal effect by attacking the metabolism of the cancerous cell. The design allows us to use amplified chemical reactivity in a controlled manner to modulate the cancerous cell at the molecular level.

We exploit metal coordination and organometallic chemistry principles to design novel potent switchable bio-catalytic metallodrugs; switchable because the activation of the drug is designed to be reversible (the drug can be inactivated *in cellula*), and bio-catalytic because catalytic transfer hydrogenation of biomolecules, leading to compromise the cancerous machinery, has been found to be crucial for the drug's lethality.

The next very important part of our research is based on the molecular study of the sequence of events that ultimately lead to cell death, i.e.; the cancerous cell fate upon the metallodrug's effect inside the cell. We do carry out cell and molecular biology studies to corroborate our understanding of the drug's effect in the cell nano-environment.

In addition, we design complexes that can be attached to selected nanomaterials to enhance the selectivity and efficiency of the drug. Our work with nanomaterials is carried out together with close collaborators inside and outside IMDEA Nanociencia.

In summary, our research seeks to exploit the physico-chemical features of the tumour cell for controlled drug activation. Our main goal is to produce new metallo-organic drugs that can exert bio-catalytic activity inside human cancer cells to break their finely tuned homeostasis in order to control cancer proliferation and stop invasion. We aim to unequivocally identify the chemical interactions of our metallodrugs with the intracellular components at the nanoscale.

Job position description

We are looking for a candidate with a strong background in synthetic organic and/or organometallic chemistry. A good understanding of analytical techniques such as NMR, UV-vis, fluorescence, and Mass Spectrometry, will be appreciated. Our candidate must have a passion for molecular and cell biology.

Research studies will focus on the synthesis of new organometallic entities and how these modulate the cancer cell machinery. The synthesis will involve the organic ligands, as well as coordination and organometallic chemistry (both ligand substitution reactions and redox chemistry involving the metal centres). Characterization techniques include NMR, MS, and powder and single crystal X-ray diffraction. Solution studies are based on NMR, UV-vis and fluorescence spectroscopy. Physico-chemical stimuli include pH and light irradiation.

The candidate will work in a wet lab, being in charge of the synthesis, characterization and aqueous (stimuli-responsive) reactivity of organometallic biocompatible drugs based on the platinum-group metals. Aqueous solution studies will be carried out to establish the activation pattern and the catalytic activity of the metal complexes. Attachment of selected metallodrugs to a variety of nanoparticles is foreseen. In addition, the candidate is expected to work in a cell culture lab, where they will learn to validate the biological effects of the metallodrugs or metallodrug-nanocarrier in a cell system, from the activation of the pro-drug to its reactivity in the intracellular nano-space.

Finally, it is foreseen that the PhD student will carry out at least one placement (usually between three and six months) in the laboratory of one of our international collaborators. Likewise, a-few-days placements at European synchrotron facilities are to be expected.

The research programme is highly interdisciplinary bringing together chemistry, cell biology and physics in the search for truly innovative metallodrugs in cancer research.