On the trail of urinary tract infections

The German government is providing about 2.4 million Euros for a new research group in infectious diseases at JMU Würzburg. Dr. Carmen Aguilar will use this grant to search for new therapeutic approaches against one of the most common and recurrent bacterial infections.

About every second woman gets a urinary tract infection once in her life, the cause for which is most often the uropathogenic bacterium Escherichia coli (UPEC). Overuse of antibiotics in the last four decades has led to bacterial strains including UPEC becoming resistant to commonly used antibiotics. Thus, new alternative treatment options are urgently needed.

In May 2022, a new junior research group started its work at the JMU on the development of innovative approaches against recurrent urinary tract infections and antibiotic-resistant UPEC strains. The Federal Ministry of Education and Research (BMBF) has now granted around 2.4 million Euros to Dr. Carmen Aguilar for her research project FiRe-UPec: Exploiting host pathways to treat antibiotic resistant uropathogenic Escherichia coli infections.

Innovative approaches against common infections

Most of the strategies to combat infectious diseases are designed to act against the pathogen itself. Given that the host response is equally essential in determining the outcome of an infection, host-based therapeutics represent an innovative approach to fight infections. “The overall goal of my project is to identify host cell factors controlling UPEC infection and to use this knowledge to develop new therapeutic approaches”, explains Dr. Carmen Aguilar.

Her group will be hosted by the ZINF (Research Center for Infectious Diseases) and the Institute of Molecular Infection Biology (IMIB). “We are excited to host the junior research group of Dr. Aguilar at the ZINF in Würzburg. In light of the continuous rise of antimicrobial resistance, her research on host pathways promises innovative new strategies to combat urinary tract infections”, says Prof. Cynthia Sharma, spokesperson of the ZINF and Chair of Molecular Infection Biology II.

Research using complex infection models

In order to mimic the site of UPEC infections, i.e. the human bladder epithelium, as realistically as possible, the research group will first generate bladder organoids – mini versions of the human organ. For this, the group of Dr. Aguilar will collaborate closely with clinicians of the University Hospital of Würzburg.

Ultimately, these complex models will also be used to test potential new active substances in a small-scale drug screen. One particular focus will be on host microRNAs (miRNAs). “microRNAs are small RNA molecules that play an important role a wide array of cellular functions by regulating host cell gene expression,” explains Aguilar.
Her research group is looking for miRNAs that exert an inhibitory effect on the infection and will be testing their suitability as new drugs. Aguilar is confident: “The manipulation of miRNAs and/or their downstream signalling pathways represents a promising approach for the treatment of urinary tract infections.”

A closer look inside a single cell

Interestingly, UPEC can replicate in some cells of the bladder epithelium but not in others. These bacteria can then be somewhat resistant to antibiotics due to their non-growing state and thus lead to recurrent infections. The team around Aguilar thus aims to determine the host cellular factors responsible for this phenotype.

In addition, the group will search for a specific cell type preferentially targeted by UPEC allowing for its successful survival and/or replication. “The reason we are looking into this, is that non-growing bacteria are a high-risk factor for the development of recurrent urinary tract infections. In order to fight these infections, it is vital to identify and understand the responsible host cell factors”, says Aguilar.

To achieve this, the group will leverage a special technique called single cell RNA-seq that enables them to determine which genes are active in every single cell by looking at their RNA content. This work will also be supported by the new Single-Cell Center Würzburg (Prof. Jörg Vogel).

Ideal scientific environment in Würzburg

"Deciphering the signalling pathways responsible for bacterial growth in bladder cells will reveal new cellular factors that could be targeted with new or already existing drugs”, says Aguilar.

The new junior research group of Dr. Carmen Aguilar is profiting from her broad expertise in the field of infection biology. Her group will closely collaborate with infection- and RNA-biologists at the JMU as well as clinicians of the University Hospital Würzburg.

She will also benefit from the strong expertise on single cell biology in Würzburg at the HIRI. Its director Prof. Jörg Vogel says: “We are very much looking forward to the collaboration with Dr. Aguilar since we share a common important goal: the fight against infectious diseases using RNA-based approaches.” Ultimately, the team is optimally suited to strive for their goal of developing innovative therapeutic approaches to fight recurrent urinary tract infections caused by antibiotic-resistant UPEC strains.

Personal details

Dr Carmen Aguilar studied biology and biotechnology at the University of Cordoba (Spain). In 2014, she completed her PhD in the field of biosciences and agri-food sciences. From 2015-2021, she pursued her postdoctoral work at the JMU Würzburg. With the funding from the BMBF, she will now start her independent junior research group at the IMIB/ZINF in Würzburg.

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