# The D<sup>2</sup>AMR group Discovery and development of Antimicrobials & Mechanisms of drug Resistance

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## **Global Context: the problem (I)**

- Antimicrobial resistance
  - Gram-positive & Gram-negative
  - 10 million deaths by 2050
- Tuberculosis
  - 10.4 million newly infected and 1.8 million died from TB
  - 1/3 of the world population infected
- Cystic Fibrosis
  - Non-tuberculosis mycobacteria
  - No current cure



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## **Global Context: the problem (II)**

- Lack of new drugs or alternative therapies
- Long and costly process from bench to bed side
- Drug Repurposing



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# **D<sup>2</sup>AMR Research Programs**

**Drug Discovery & Development of Antimicrobials** 

- Screening campaigns (chemical biology)
- Mode of action elucidation (genetics & biochemistry)
- Pre-clinical development (in vitro & in vivo)
- **PKPD** modelling (dosing optimization)
- **Target diseases** 
  - Tuberculosis / Buruli ulcer / Yaws (neglected diseases)
  - Cystic Fibrosis (non-tuberculosis mycobacterias)
  - Antimicrobial resistance (WHO priority List)

**Therapeutic strategies** 

- Synergy & repurposing
- Medicinal Chemistry campaings
- De novo screening from natural sources
- Nanotechnology for co-delivery of synergistic partners

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# **On-going projects**

- The silent phenotype in Mycobacterium tuberculosis: persistence (Spanish Government- MINECO)
- Role of Pseudomonas aeruginosa biofilms in exacerbations in patients with bronchiectasis with and without Chronic Obstructive Pulmonary Disease (Spanish Government – CIBERES)
- NAREB: Nanoparticles for Antibiotic Resistant Emerging Bacteria Pathogens. (FP7 / European Commission).
- BLMs4TB: Predicting optimal partners, combinatorial dosing schedules and clinical outcomes of beta-lactams using PKPD and mechanistic in vitro models. (TCOLF/ GSK/H2020).
- SynCF: Novel drug repositioning strategies for difficult to treat CF infections. (ESCMID).
- Discovery and development of novel anti-bacterial drugs. (CDRD/UBC).
- **Discovery and development of tigecycline enhancer in Klebsiella pneumoniae** (Shenzhen People's Hospital).
- Avermectins and milbemycins as anti-mycobacterial agents. (US 9,308,215 B2).

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#### **Strategic Partners**

- Tres Cantos Open Lab Foundation (TCOLF)
- GlaxoSmithKline (GSK) I+D, SL DDW campus
- University of British Columbia (UBC)
- Center for Drug Research & Development (CDRD)
- Shenzhen People's Hospital
- Ramon y Cajal Hospital, Madrid

### trescantos Open Lab Foundation







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- Government of Aragon

- European Society for Clinical Microbiology and Infectious Diseases
- TCOLF / GSK

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