

Team name and photography:

Animal Health group of IdAB-CSIC - Brucellosis and other bacterial zoonoses

Brief description:

The Animal Health group of IdAB-CSIC led by Dr. María Jesús Grilló works in the field of brucellosis and other zoonotic bacterial pathogens, with two main lines of research:

1. The brucellosis line (in which Dr. Grilló is working for more than 28 years) has been continuously funded since its inception at IdAB-CSIC in 2010. We have carried out recent studies dealing with prophages in different *Brucella* strains, under different *in vitro* and *in vivo* growth conditions. As a result, we have identified certain new *Brucella* phage sequences, which could be of great interest for understanding the pathogenesis of this bacterium. We will continue this line of research aimed to develop molecular and therapeutic tools with multiple applications to solve existing practical problems in the field of brucellosis, in the context of the new project PID2022-139200OB-C21 (2023-2026) awarded (provisional resolution) in the last call of the Ministry of Science - AEI of Spain.
2. In the line of other bacterial pathogens, the group actively collaborates with different groups of research and biotechnological companies, contributing in the evaluation in animals of phage or derived recombinant proteins, as alternative therapeutic targets to the use of antibiotics. We have developed different mouse models, such as mastitis, lethality, sealed catheter implanted subcutaneously, respiratory or oral infections, directed to treat bacterial infections such as *Staphylococcus aureus*, *S. epidermidis*, *Salmonella* spp., *Mycoplasma*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, among other.

Group Members:

- Dr. María Jesús Grilló is PI of the group, has a Ph.D. in Veterinary Medicine and is a scientific researcher of the CSIC, with more than 28 years of experience in microbiology and animal health; she has been PI and coordinator of several R&D projects, promoter of a *spin-off* of the CSIC, and inventor of 8 technological transfer contributions (7 patents, 1 Trade Mark).
- Dr. Victoria Garrido has a Ph.D. in Biology, with a double degree in Biology and Biochemistry from the University of Navarra (UNAV); she is a postdoctoral researcher contracted since 2009 in different projects of the CSIC-IdAB Animal Health Group. Dr. Garrido has extensive experience in bacterial zoonoses caused by different pathogens (*Salmonella*, *Listeria*, *Mycoplasma*, *Staphylococcus*, *Acinetobacter*, *Pseudomonas*, *Klebsiella*, among others), in the field of antimicrobial resistance, detection of mobile genetic elements and development of diagnostic tests, as well as in the development of animal experimental models to evaluate the safety and efficacy of different treatments.
- Dr. Ana Zabalza has a Ph.D. in Biology, with a double degree in Biology and Biochemistry from the University of Navarra (UNAV); she is a postdoctoral researcher contracted since 2011 in different projects of the IdAB-CSIC Animal Health Group; Dr. Zabalza has experience in the field of brucellosis, vaccine development and diagnostic tools.

Research topics:

Zoonoses, *Brucella*, bacteriophages, therapy, vaccines, animal models, diagnostic tools.

Recent articles: (last 5 years)

- *Engineered live bacteria suppress Pseudomonas aeruginosa infection in mouse lung and dissolve endotracheal-tube biofilms.* **2023.** Mazzolini R, Rodríguez-Arce I, Fernández-Barat L, Piñero-Lambeck C, Garrido V, Rebollada-Merino A, Motos A, Torres A, Grilló MJ, Serrano L, Lluch-Senar M. **Nature Biotechnology**, 19. doi: 10.1038/s41587-022-01584-9.
- *Vaccine properties of Brucella melitensis 16MΔwzm and reactivation of placental infection in pregnant sheep.* **2023.** Zabalza-Baranguá A, Poveda-Urkixo I, Mena-Bueno S, Ramírez GA, De Bolle X, Grilló MJ. **Vaccine**, 41(9):1554-1566. doi: 10.1016/j.vaccine.2023.01.017.
- *BruSIC: a novel selective medium for the primary isolation of Brucella in veterinary samples.* **2022.** Mena-Bueno S, Poveda-Urkixo I, Asensio D, Echarte I, Zabalza-Baranguá A, Grilló MJ. **Microbiology Spectrum**, 10(6): e0175922. doi: 10.1128/spectrum.01759-22.
- *Brucella melitensis Wzm/Wzt System: Changes in the Bacterial Envelope Lead to Improved Rev1Δwzm Vaccine Properties.* **2022.** Mena-Bueno S, Poveda-Urkixo I, Irazoki O, Palacios L, Cava F, Zabalza-Baranguá A, Grilló MJ. **Front Microbiology**, 13:908495. doi: 10.3389/fmicb.2022.908495.
- *Kinetics of Placental Infection by Different Smooth Brucella Strains in Mice.* **2022.** Poveda-Urkixo I, Ramírez GA, Grilló MJ. **Pathogens**, 11(3):279. doi: 10.3390/pathogens11030279.
- *Brucella abortus S19 GFP-tagged vaccine allows the serological identification of vaccinated cattle.* **2021.** Chacón-Díaz C, Zabalza-Baranguá A, San Román B, Blasco JM, Iriarte M, Salas-Alfaro D, Hernández-Mora G, Barquero-Calvo E, Guzmán-Verri C, Chaves-Olarte E, Grilló MJ, Moreno E. **PLoS ONE**, 16(11): e0260288. doi: 10.1371/journal.pone.0260288. eCollection 2021.
- *Engineering a genome-reduced bacterium to eliminate Staphylococcus aureus biofilms in vivo.* **2021.** Garrido V, Piñero-Lambeck C, Rodríguez-Arce I, Paetzold B, Ferrar T, Weber M, García-Ramallo E, Gallo C, Collantes M, Peñuelas I, Serrano L, Grilló MJ, Lluch-Senar M. **Molecular Systems Biology**, 17(10): e10145. doi: 10.15252/msb.202010145.
- *Prevalence of Salmonella in Free-Range Pigs: Risk Factors and Intestinal Microbiota Composition.* **2021.** Garrido V, Migura-García L, Gaitán I, Arrieta-Gisasola A, Martínez-Ballesteros I, Fraile L, Grilló MJ. **Foods**, 10(6):1410. doi: 10.3390/foods10061410.
- *Genotyping Study of Salmonella 4,[5],12:i:- Monophasic Variant of Serovar Typhimurium and Characterization of the Second-Phase Flagellar Deletion by Whole Genome Sequencing.* **2020.** Arrieta-Gisasola A, Atxaerandio-Landa A, Garrido V, Grilló MJ, Martínez-Ballesteros I, Laorden L, Garaizar J, Bikandi J. **Microorganisms**, 8(12):2049. doi: 10.3390/microorganisms8122049.
- *Phage Lytic Protein LysRODI Prevents Staphylococcal Mastitis in Mice.* **2020.** Gutiérrez D, Garrido V, Fernández L, Portilla S, Rodríguez A, Grilló MJ, García P. **Frontiers Microbiology**, 11:7. doi: 10.3389/fmicb.2020.00007. eCollection 2020.
- *Salmonella Infection in Mesenteric Lymph Nodes of Breeding Sows.* **2020.** Garrido V, Sánchez S, San Román B, Fraile L, Migura-García L, Grilló MJ. **Foodborne Pathogens and Disease**, 17(6):411-417. doi: 10.1089/fpd.2019.2708.

- *Rapid and specific detection of Salmonella infections using chemically modified nucleic acid probes.* **2019.** Machado I, Garrido V, Hernández LI, Botero J, Bastida N, San-Román B, Grilló MJ, Hernández FJ. **Anales Chimica Acta**, 25; 1054:157-166. doi: 10.1016/j.aca.2018.12.027.
- *GFP tagging of Brucella melitensis Rev1 allows the identification of vaccinated sheep.* **2019.** Zabalza-Baranguá A, San-Román B, Chacón-Díaz C, de Miguel MJ, Muñoz PM, Iriarte M, Blasco JM, Grilló MJ. **Transboundary and Emerging Diseases**, 66(1):505-516. doi: 10.1111/tbed.13053.
- *Relationship between Salmonella infection, shedding and serology in fattening pigs in low-moderate prevalence areas.* **2018.** San Román B, Garrido V, Sánchez S, Martínez-Ballesteros I, Garaizar J, Mainar-Jaime RC, Migura-Garcia L, Grilló MJ. **Zoonoses and Public Health**, 65(5):481-489. doi: 10.1111/zph.12453.
- *Multidrug resistant Salmonella enterica isolated from conventional pig farms using antimicrobial agents in preventative medicine programmes.* **2018.** Cameron-Veas K, Fraile L, Napp S, Garrido V, Grilló MJ, Migura-Garcia L. **Veterinary Journal**, 234:36-42. doi: 10.1016/j.tvjl.2018.02.002.
- *Identification of lptA, lpxE, and lpxO, Three Genes Involved in the Remodeling of Brucella Cell Envelope.* **2018.** Conde-Álvarez R, Palacios-Chaves L, Gil-Ramírez Y, Salvador-Bescós M, Bárcena-Varela M, Aragón-Aranda B, Martínez-Gómez E, Zúñiga-Ripa A, de Miguel MJ, Bartholomew TL, Hanniffy S, Grilló MJ, Vences-Guzmán MÁ, Bengoechea JA, Arce-Gorvel V, Gorvel JP, Moriyón I, Iriarte M. **Frontiers Microbiology**, 10(8): 2657. doi: 10.3389/fmicb.2017.02657. eCollection 2017.

Research projects:

Public funding: (last 5 years)

- *Brucella* placental pathogenesis and vaccines development from a new molecular perspective in brucellosis (*BruPatho*). Funding entity: Ministerio de Ciencia e Innovación - AEI (PID2022-139200OB-C21). Provisional resolution. 2023-2026.
- Desarrollo de enzibióticos frente a infecciones respiratorias por *Staphylococcus aureus* (*Respi-Staph-Out*). Funding entity: Dpto. de Desarrollo Económico y Empresarial (Servicio de Innovación y Transferencia del Conocimiento) de Gobierno de Navarra. 2022-2024.
- Nuevos desarrollos y aplicaciones de un dispositivo para la detección de bacterias patógenas mediante resonancia plasmónica (*BactoPlus*). Funding entity: Dpto. de Universidad, Innovación y Transformación Digital de Gobierno de Navarra (PC021-022-023). 2020-2022
- The *Brucella* Wzm/Wzt two-component system: molecular studies, host-pathogen interactions in sheep and applications in *B. suis* (*Bru2Comp*). Funding entity: MINECO-CICYT (RTI-2018-098658-B-C21). 2019-2022.
- “Brucellosis Vaccine Global Prize”: Evaluación de la vacuna BGV1 (*BGV-Prize*). Funding entity: Departamento de Desarrollo Económico y Empresarial (Servicio de Innovación y Transferencia del Conocimiento) del Gobierno de Navarra (PT2018-040 y PT2019-007). 2018-2019.
- Reto DIVA-GFP contra la brucelosis: desarrollo de una proteína GFP para registro como medicamento veterinario y tests de diagnóstico GFP asociados. Funding entity MINECO- Programa RETOS-COLABORACIÓN 2015 (RTC-2015-3618-1). 2016-2018.

- Brucellosis: Diagnostic tests and DIVA vaccines against *Brucella ovis* and *Brucella suis* (*Bru-DivaOS*). Funding entity: MINECO (AGL2014-58795-C4-2-R). 2015-2018.
- Identificación de nucleasas específicas de *Brucella* y *Salmonella* para el desarrollo de nuevos métodos de diagnóstico y cuantificación de ambos patógenos, mediante el diseño de sondas de oligonucleótidos (*BactoProbes*). Funding entity: Departamento de Desarrollo Económico (Servicio de Innovación y Transferencia del Conocimiento) del Gobierno de Navarra (PT2016-071, PT2017-031, PC2018-068; PC2019-055). 2016-2019.

R&D contracts: (last 5 years)

- Evaluación en ratones BALB/c de la eficacia de vacunas de subunidad frente a infección virulenta por *Brucella abortus*. Funding entity: Centro de Ingeniería Genética y Biotecnología (CIGB; Cuba). 2023-2025.
- Evaluación en ratones de la eficacia antimicrobiana de distintas endolisinas obtenidas por ingeniería sintética. Funding entity: Telum Therapeutics SL (Navarra). 2022-2023.
- Nuevo sistema automatizado de siembra en masa para el diagnóstico microbiológico en agentes contaminantes. Funding entity: Reactivos Para Diagnóstico SL (RPD; Barcelona). 2022-2024.
- Characterization of different *Mycoplasma* constructs in mice lungs. Funding entity: Pulmobiotics SL (Barcelona). 2020-2022.
- Assays to evaluate the virulence/pathogenicity of certain bacteria in the lungs of mice and the activity of selected constructions against bacterial biofilms *in vivo*. Funding entity: Fundación Centre de Regulación Genómica (CRG; Barcelona). 2017-2020.
- *In vivo* test of biosafety circuits to limit *Mycoplasma pneumoniae* growth after induction of killing function of the circuits. Funding entity: CRG - Imperial College of London (UK). 2020-2021.
- Tareas de apoyo al proyecto *BGV-Prize*. Funding entity: Brucella GreenVac SL (Navarra). 2018-2019.

Doctoral Thesis: (last 10 years)

- Sara Mena Bueno. 30/03/2023. Estudio del sistema Wzm/Wzt en *Brucella* y evaluación del candidato vacunal Rev1Δwzm frente a la brucelosis ovina.
- Irati Poveda Urkixo. 28/7/2022. Estudios de patogénesis placentaria por *Brucella* y caracterización molecular de *Brucella suis* bv2.
- Ana Zabalza Baranguá. 28/7/2017. Desarrollo y evaluación de nuevas vacunas y tests de diagnóstico frente a la brucelosis ovina, para la identificación de los animales vacunados.
- Samanta Sánchez Alarcón. 29/5/2015. Salmonelosis porcina en Navarra: situación epidemiológica y sanitaria del porcino de engorde, en el contexto europeo.
- Pedro Soler Llorens. 4/7/2014. Desarrollo de nuevas vacunas frente a *Brucella ovis*: Estudio de genes implicados en la síntesis del núcleo del lipopolisacárido.

Web site: <https://www.idab.csic.es/>