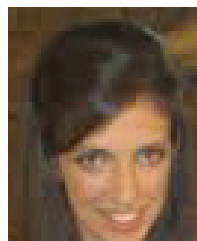
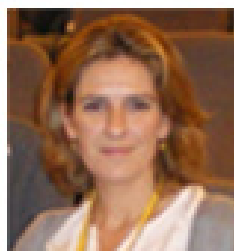
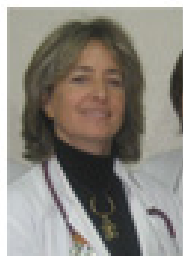
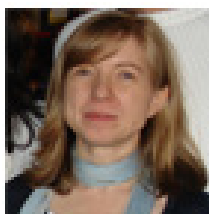




3.3.7 Drug Hypersensitivity and Innate Immune Response Group



Publications: 12 | Q1: 9

COMPOSITION

Teresa Bellón Heredia.

Investigadora Senior (Contrato Miguel Servet -I2). Jefe de laboratorio. FIBHULP

- **María del Rosario Cabañas Moreno.** Facultativo Especialista de Área en Alergología. Hospital Universitario La Paz
- **Sofía Caiqin Linares Reyes.** Investigadora Predoctoral. FIBHULP
- **Celia Martínez Prieto.** Técnico de Grado Superior. Hospital Universitario La Paz
- **Beatriz Sanz Minguela.** Técnico de Grado Superior. Hospital Universitario La Paz
- **Guillermo Servera Negre.** Facultativo Especialista en Dermatología Médico-Quirúrgica y Venereología. Hospital Universitario La Paz

STRATEGIC OBJETIVES

- Cutaneous adverse drug reactions are unpredictable and represent a plethora of skin diseases with various degrees of severity. The spectrum ranges from mild to potentially fatal multisystem maladies. Those of most concern are usually referred to as severe cutaneous adverse reactions (SCARs), and include acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS), also known as drug induced hypersensitivity syndrome or hypersensitivity syndrome (DIHS/HSS), Stevens-Johnson's syndrome (SJS), and toxic epidermal necrolysis (TEN). Among them, SJS and TEN are the most severe clinical entities and are nowadays considered as variants of the same disease characterized by keratinocyte necrosis and epidermal detachment with the formation of subepidermal bullae. From the immunopathogenic point of view, SCARs are T-cell mediated type IV hypersensitivity reactions. However, T cells can orchestrate different types of immune responses and this functional heterogeneity has led to a further sub-classification into type IVa-IVd hypersensitivity that considers the distinct cytokine production pattern by T cell subpopulations, and emphasizes the participation of different effector cells causing inflammation and tissue damage. Current knowledge supports the active participation of cytotoxic lymphocytes in different clinical entities.
- Our project aims to a better understanding of the immune mechanisms underlying the etiopathogenesis of these diseases. The study is performed in the framework of the consortium PIELenRed (Plataforma interdisciplinar para el estudio de reacciones cutáneas graves en red) integrated by researchers belonging to different hospitals in Madrid.
- Reactivation of latent herpesvirus has been described during the development of some of the previously mentioned clinical entities. In order to improve our understanding of the behaviour of the immune system during viral replication, collaboration has been established with the Kidney Transplant Unit (Nephrology Service, HULP). Kidney transplant recipients are being followed immediately before and after transplant in order to identify patients with active CMV replication.
- General objectives for the next 5 years
- The main objectives are:
 - I. Biobanking of samples of severe cutaneous adverse reactions to medications (DRESS, AGEP and SJS/TEN) associated to the registry PIELenRed, and integrated in the international registry RegiSCAR.
 - II. To investigate in vitro test for drug causality assessment.
 - III. To explore the involvement of the innate immune response (in particular natural cytotoxic activity) during the development of SCARs.
 - IV. Identification of biomarkers of susceptibility.
 - V. To find biomarkers for disease and response to treatments.
 - VI. To explore the potential of microRNAs in SJS/TEN as biomarkers of disease and of response to treatments, as well as their relationship with pathogenic mechanisms.



RESEARCH LINES

- Biobanking of biological samples from patients with severe cutaneous adverse reactions to medications (DRESS, AGEP and SJS/TEN).
- Development and evaluation of in vitro tests for drug causality assessment.
- Identification of biomarkers of susceptibility.
- Involvement of NK receptors in the etiopathogenesis of Stevens-Johnson syndrome /Toxic epidermal necrolysis (SJS/TEN).
- Differential analysis of the cytokine pattern involved in different SCARs (AGEP, DRESS and SJS/TEN).
- Analysis of miRNAs as biomarkers of disease and response to treatments.

RESEARCH ACTIVITY

Final Degree Theses

- **Linares Reyes SC.** Regulación de la expresión de IL15 e IL15RA en fibroblastos de piel: Relevancia para el tratamiento de pacientes con Síndrome de Stevens-Johnson /necrólisis epidérmica tóxica. [dissertation]. *Tenerife : Universidad de la Laguna: 2023(01/06/2023). Director: Bellón Heredia T.*

Publications

- **Angelo KM, Smith T, Camprubi-Ferrer D, Balerdi-Sarasola L, Menéndez MD, Servera-Negre G, Barkati S, Duvignaud A, Huber KLB, Chakravarti A, Bottieau E, Greenaway C, Grobusch MP, Pedro DM, Asgeirsson H, Popescu CP, Martín C, Licitra C, de Frey A, Schwartz E, Beadsworth M, Lloveras S, Carsten C, Guagliardo SAJ, Whitehill F, Huits R, Hamer DH, Kozarsky P, Libman M.** Epidemiological and clinical characteristics of patients with monkeypox in the GeoSentinel Network: a cross-sectional study. *Lancet Infect Dis.* 2023; 23(2): 196-206. Article. IF: 36.4; D1
- **Balas A, Moreno-Hidalgo MA, de la Calle-prieto F, Vicario JL, Arsuaga M, Trigo E, de Miguel-Buckley R, Bellón T, Díaz-Menéndez M.** Coronavirus-19 disease risk and protective factors associated with HLA/KIR polymorphisms in Ecuadorian patients residing in Madrid. *Hum Immunol.* 2023; 84(11): 571-7. Article. IF: 3.1; Q3

- **Herranz-Pinto P, Alonso-Pacheco ML, Feltes-Ochoa R, Mayor-Ibarguren A, Servera-Negre G, Busto-Leis JM, González-Fernández MA, Herrero-Ambrosio A.** Real-world performance of a new strategy for off-label use of guselkumab in moderate to severe psoriasis: super-responder patients as the epitome of efficacy and optimisation. *Clin Drug Invest.* 2023; 43(7): 517-527. Article. IF: 2.9; Q2
- **Marks ME, Botta RK, Abe R, Beachkofsky TM, Boothman I, Carleton BC, Chung WH, Cibotti RR, Dodiuk-Gad RP, Grimstein C, Hasegawa A, Hoofnagle JH, Hung SI, Kaffenberger B, Kroshinsky D, Lehloenya RJ, Martín-Pozo M, Micheletti RG, Mockenhaupt M, Nagao K, Pakala S, Palubinsky A, Pasieka HB, Peter J, Pirmohamed M, Reyes M, Saeed HN, Shupp J, Sukasem C, Syu JY, Ueta M, Zhou L, Chang WC, Becker P, Bellon T, Bonnet K, Cavalleri G, Chodosh J, Dewan AK, Dominguez A, Dong XZ, Ezhkova E, Fuchs E, Goldman J, Himed S, Mallal S, Markova A, McCawley K, Norton AE, Ostrov D, Phan M, Sanford A, Schlundt D, Schneider D, Shear N, Shinkai K, Tkaczyk E, Trubiano JA, Volpi S, Bouchard CS, Divito SJ, Phillips EJ.** Updates in SJS/TEN: collaboration, innovation, and community. *Front Med (Lausanne).* 2023; 10: 1213889. Review. IF: 3.1; Q1
- **Narváez-Fernández EJ, Entrala A, Nin-Valencia A, Mir-Ihara P, Losantos-García I, Domínguez-Ortega J, González-Fernández MA, Quirce S, Hernández-Cano N, Cabañas R, Caballero T.** Long-term omalizumab

in elderly patients with chronic urticaria: is it a safe therapy?. *Int Arch Allergy Imm.* 2023; 184(10): 1003-9. Article. IF: 2.5; Q3

- **Nin-Valencia A, Domínguez-Ortega J, Cabañas R, Sánchez H, Fiandor A, Lluch M, Ramírez E, Gómez-Traseira C, Rodríguez A, González-Muñoz M.** The lymphocyte transformation test in delayed hypersensitivity reactions induced by ibuprofen and/or metamizole. *J Invest Allerg Clin.* 2023; 33(1): 52-3. Editorial Material. IF: 6.1; Q1
- **Nin-Valencia A, Fiandor A, Lluch M, Quirce S, Caballero T, Heredia RR, González-Muñoz M, Caballero ML, Cabañas R.** Safe administration of Sars-Cov-2 vaccine after desensitization to a biologic containing polysorbate 80 in a patient with polyethylene glycol-induced severe anaphylaxis and sensitization to polysorbate 80. *J Invest Allerg Clin.* 2023; 33(2): 151-3. Article. IF: 6.1; Q1
- **Olsson-Brown A, Yip V, Ogiji ED, Jolly C, Ressel L, Sharma A, Bergfeld W, Liu X, Khirwadkar N, Bellon T, Dickinson A, Ahmed S, Langton A, Watson R, Pirmohamed M, Carr DF.** TNF- α -mediated keratinocyte expression and release of matrix metalloproteinase 9: putative mechanism of pathogenesis in stevens-johnson syndrome/toxic epidermal necrolysis. *J Invest Dermatol.* 2023; 143(6): 1023-30. Article. IF: 5.7; D1
- **Rodríguez-Pérez R, de las Vecillas L, Cabañas R, Bellon T.** Tools for etiologic diagnosis of drug-induced allergic conditions. *Int J Mol Sci.* 2023; 24(16): 12577. Review. IF: 4.9; Q1
- **Sobral-Costas TG, Escudero-Tornero R, Servera-Negre G, Bernardino JI, Arroyo AG, Díaz-Menéndez M, Busto-Leis JM, Álvarez PR, Pinto PH, Cudos ES.** Human monkeypox outbreak: Epidemiological data and therapeutic potential of topical cidofovir in a prospective cohort study. *J Am Acad Dermatol.* 2023; 88(5): 1074-82. Article. IF: 12.8; D1
- **Sobral-Costas TG, Escudero-Tornero R, Servera-Negre G, Bernardino JI, Arroyo AG, Díaz-Menéndez M, Busto-Leis JM, Álvarez PR, Pinto PH, Cudos ES.** Topical cidofovir in monkeypox: our experience. Comment on Monkeypox: is topical cidofovir a good idea? *Clin Exp Dermatol.* 2023; 48(6): 700-1. Letter. IF: 3.7; Q1
- **Zingoni A, Bellón T.** Editorial: Women in NK and innate lymphoid cell biology. *Front Immunol.* 2023; 14: 1157166. Editorial Material. IF: 5.7; Q1

Research projects

- **Bellón Heredia T.** Contrato Miguel Servet Categoría B (CES06/016). ISCIII. 2007-2025. *Managment centre: FIBHULP*
- **Bellón Heredia T.** Impacto de los inhibidores de calcineurina sobre linfocitos efectores citotóxicos en síndrome de Stevens-Johnson/ necrólisis epidérmica tóxica de análisis de il-15 como biomarcador (PI18/00718). ISCIII. 2019-2023. *Managment centre: FIBHULP*
- **Bellón Heredia T.** Creación de un centro de referencia para el estudio de los mecanismos implicados en las reacciones de hipersensibilidad a las membranas de hemodíalisis basadas en polysulfona (PI-3009). Nipro Euope NV. 2017-Ongoing. *Managment centre: FIBHULP*
- **de las Vecillas Sánchez L.** Estudio de la inmunomodulación celular inducida en las desensibilizaciones a quimioterápicos tras reacciones inmediatas y tardías. Sociedad Española de Alergología e Inmunología Clínica (SEAIC). 2022-2024. *Managment centre: Fundación SEAIC*
- **Bellón Heredia T.** ELISpot como método diagnóstico para identificación del fármaco causal en pacientes con reacciones graves de hipersensibilidad cutánea a medicamentos: comparación con TTL FIBHULP. 2022-2023. *Managment centre: FIBHULP*

Patents and trademarks

- **Selgas Gutiérrez R, Bellón Heredia T, Rodríguez Sanz AI, Álvarez Builla J, Vaquero López JJ, Sánchez Alonso P, Alajarín Fernández R, inventors; FIBHULP, Universidad de Alcalá, assignees.** Use of compounds derived from salts of pyridazine[1',6':1,2]pyrido[3,4-b]indolinium as anti-inflammatory agents. P201331143, PCT/ES2014/070603; 2013 July 25.
- **Selgas Gutiérrez R, Bellón Heredia T, Rodríguez Sanz AI, Álvarez Builla J, Vaquero López JJ, Sánchez Alonso P, Alajarín Fernández R, inventors; FIBHULP, Universidad de Alcalá, assignees.** Use of compounds derived from salts of piridazine[3,2-b]benzimidazolium as anti-inflammatory agents. P201430411, PCT/ES2014/070603; 2013 July 25.