

SWISS LIVER



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Research Progress Report: Primary Biliary Cholangitis in the Context of Systemic Autoimmunity

Name of Grantee: Mirjam Kolev

Date: 19.04.2024

Summary / Brief outline of topic

- 1) PBC is very often associated with extrahepatic autoimmunity, first of all Sjögren's disease. However, data on the prevalence of other autoimmune diseases is scarce. Furthermore, there is conflicting data, on whether the presence of Sjögren's disease might influence prognosis. Therefore, we are doing a retrospective analysis on primary biliary cholangitis and extrahepatic autoimmunity; prevalence and impact on progression of liver disease.
- 2) Diagnosis of PBC relies heavily on the presence of autoantibodies (AMA M2, gp210 and sp100). However, about 5-10% are seronegative. We are doing a feasibility analysis of anti-Hexokinase 1 and anti-Kelch-like 12 Peptide as novel antibodies in PBC.
- 3) PBC and Sjögren's disease share many epidemiological and pathophysiological similarities. Inflammatory pathways are not well characterized in both diseases. Therefore, we set up a prospective study in collaboration with the clinic of Rheumatology, for a prospective study investigating clinical presentation, inflammatory pathways in saliva, blood and biopsies.

Activities

- 1) 237 patients entered into RedCap database. Controlling data entry/data completion. Analysis and writing of the manuscript.
- 2) Data entry in data base completed. Samples shipped to the USA for measurement. Measurement because of the COVID-pandemia still pending (new calibration of antibody measurements necessary).
- 3) Patient inclusion started in January 2024.

Results Not applicable.

Discussion Not applicable.

Achievements (Grants / Prizes / Publications)

Grants:

- 08/2022-07/2023 Doc.Mobility Grant UniBE: 55'000.- PhD-salary.
- 09/2023 Strategische Förderungs Board Inselspital, SF Call: Functional impact of environmental factors on Sjögren's syndrome and primary biliary cholangitis; 750'000.- CHF, of those 93'690.- CHF for 20% protected research time for three years for Mirjam Kolev.
- 11/2023 KinderInsel Stiftung: Phenotyping antigens of antinuclear antibodies in juvenile autoimmune hepatitis for improved diagnosis; 10'000.- CHF for materials.
- 03/2024 Nachwuchsförderungs-Grant für patientenorientierte Forschung, Dekanat für Lehre und Forschung, Inselspital: 80'000.- for 20% protected research time for two years for Mirjam Kolev.

Prizes:

- Award for one of the three best abstracts in Hepatology at the Swiss Congress of Gastroenterology and Hepatology 2023

Publications:

Hepatic safety and efficacy of immunomodulatory drugs used in patients with autoimmune hepatitis.

*Benedetta Terzioli Beretta-Piccoli, Gustav Buescher, George Dalekos, Anja Geerts, Nasser Semmo, **Mirjam Kolev**, Eleonora De Martin, Maciej K. Janik, João Madaleno, Milica Stojkovic Lalosevic, Jérôme Dumortier, Thomas Vanwolleghem, Ida Schregel, Silja Steinmann, Florence Lacaille, Marcial Sebode.*

J Autoimmun. 2023 Sep 14;140:103113. doi: 10.1016/j.jaut.2023.103113.

Belimumab treatment in autoimmune hepatitis and primary biliary cholangitis - a case series

Mirjam Kolev, Adela-Cristina Sarbu, Burkhard Möller, Britta Maurer, Florian Kollert, Nasser Semmo. J Transl Autoimmun. 2023 Jan 14;6:100189.

Mycophenolate mofetil as second line treatment in autoimmune hepatitis - A retrospective single center analysis

Mirjam Kolev, Stefan Diem, Lara Diem, Susana G Rodrigues, Annalisa Berzigotti, Guido Stirnimann, Nasser Semmo. *J Transl Autoimmun.* 2022 Nov 19;5:100172

Histological and serological features of acute liver injury after SARS-CoV-2 vaccination

Greta Codoni, Theresa Kirchner, Bastian Engel, Alejandra Maria Villamil, Cumali Efe, Albert Friedrich Stättermayer, Jan Philipp Weltzsch, Marcial Sebode, Christine Bernsmeier, Ana Lleo, Tom Jg Gevers, Limas Kupčinskas, Agustin Castiella, Jose Pinazo, Eleonora De Martin, Ingrid Bobis, Thomas Damgaard Sandahl, Federica Pedica, Federica Invernizzi, Paolo Del Poggio, Tony Bruns, **Mirjam Kolev**, Nasser Semmo, Fernando Bessone, Baptiste Giguët, Guido Poggi, Masayuki Ueno, Helena Jang, Gülsüm Özlem Elpek, Neşe Karadağ Soylu, Andreas Cerny, Heiner Wedemeyer, Diego Vergani, Giorgina Mieli-Vergani, M Isabel Lucena, Raul J Andrade, Yoh Zen, Richard Taubert, Benedetta Terziroli Beretta-Piccoli. *JHEP Rep.* 2022 Oct 13;5(1):100605.

Rational development and application of biomarkers in the field of autoimmunity: A conceptual framework guiding clinicians and researchers

Mirjam Kolev, Michael P Horn, Nasser Semmo, Michael Nagler. *J Transl Autoimmun.* 2022 Mar 6;5:100151.

Adult form of Langerhans cell histiocytosis with pulmonary and hepatic involvement mimicking malignancy in a patient with chronic hepatitis C infection

Moulet B, **Kolev M**, Ebner L, Langer R, Gräni C, Obmann V, Maurer M, Semmo N, Christe A, and Huber AT. *Radiol Case Reports* 2021 Feb; 16(2): 327–333.

Outlook / Next steps

Projects:

- Writing two manuscripts from the Paris-data: 1) PSC with features of AIH: phenotyping and prognosis; 2) Prognostic factors in patients with PSC
- Inclusion of patients with PBC with or without sicca-symptoms or Sjögren's disease into the Bernese Sicca trial.
- Finishing the data entry/analysis on PBC and extrahepatic autoimmunity.
- As soon as the novel antibodies samples are measured: analysis and writing of the manuscript.
- Thesis defense by the end of 2024 (Change of doctoral agreement with inclusion of the Thy-1 project and the PSC-data in order to finish the PhD this year)

Manuscripts with advanced status:

Delineating Autoimmune Hepatitis from Drug-Induced Liver Injury: The Role of Anti-Nucleosome and Anti-Histone Antibodies

Mirjam Kolev, Guido Stirnimann, Henning Nilius, Martin Wartenberg, Juliette Schlatter, Michèle Freiburghaus, Michael Nagler, Michael P. Horn and Nasser Semmo

Submitted to *Liver International* April 2024

Correlation of Thy-1 Expression and soluble Thy-1 with Fibrosis Severity in Primary Biliary Cholangitis and Metabolic Dysfunction-Associated Fatty Liver Disease

Mirjam Kolev, Anja Saalbach, Rahel Bütikofer, Florian Kollert, Matteo Montani and Nasser Semmo

In internal review process

Elevated polyreactive immunoglobulin G in immune mediated liver injuries with the need for immunosuppressive therapy

Theresa Kirchner, George N. Dalekos, Kalliopi Zachou, Mercedes Robles-Díaz, Raúl J. Andrade, Marcial Sebode, Ansgar Lohse, Maciej K. Janik, Piotr Milkiewicz, **Mirjam Kolev**, Nasser Semmo, Tony Bruns, Tom Jg Gevers, Benedetta Terziroli Beretta-Piccoli, Heiner Wedemeyer, Elmar Jaeckel, Richard Taubert and Bastian Engel

In internal review process

Acute liver injury with autoimmune features following SARS-CoV-2 vaccination in an ERN/IAIHG cohort: autoimmune hepatitis versus drug-induced autoimmune-like hepatitis

Donald Malino, Greta Codoni, Theresa Kirchner, Bastian Engel, Alejandra Maria Villamil, Cumali Efe, Albert Friedrich Stättermayer, Jan Philipp Weltzsch, Marcial Sebode, Christine Bernsmeier, Ana Lleo, Tom JG Gevers, Limas Kupčinskas, Agustin Castiella, Jose Pinazo, Eleonora De Martin, Ingrid Bobis, Thomas Damgaard Sandahl, Federica Pedica, Federica Invernizzi, Paolo Del Poggio, Tony Bruns, **Mirjam Kolev**, Nasser Semmo, Fernando Bessone, Baptiste Giguët, Guido Poggi, Masayuki Ueno, Helena Jang, Gülsüm Özlem Elpek, Neşe Karadağ Soylu, Andreas Cerny, Heiner Wedemeyer, Diego Vergani, Giorgina Mieli-Vergani, M. Isabel Lucena, Raul J Andrade, Yoh Zen, Richard Taubert, Benedetta Terziroli Beretta-Piccoli

In internal review process