



HAL
open science

Early life stress induces type 2 diabetes at adulthood in male mice

Hanna Ilchmann-Diounou, Maïwenn Olier, Corinne Lencina, Sandrine Ellero-Simatos, Ambre Riba, Cherryl Harkat, Caroline Sommer, Hervé Guillou, Laurence Guzylack-Piriou, Vassilia Theodorou, et al.

► **To cite this version:**

Hanna Ilchmann-Diounou, Maïwenn Olier, Corinne Lencina, Sandrine Ellero-Simatos, Ambre Riba, et al.. Early life stress induces type 2 diabetes at adulthood in male mice. 10. International Meeting of Pediatric Endocrinology, Sep 2017, Washington, United States. hal-01603069

HAL Id: hal-01603069

<https://hal.science/hal-01603069>

Submitted on 5 Jun 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Early life stress induces type 2 diabetes at adulthood in male mice

Hanna Ilchmann, Maiwenn Olier, Corinne Lencina, Sandrine Ellero-Simatos, Michèle Nankap, Ambre Riba, Caroline Sommer, Hervé Guillou, Laurence Guzylack-Piriou, Vassilia Théodorou, Sandrine Ménard

The incidence of metabolic disorders is increasing worldwide. Besides diet and life style habits, epidemiological studies highlighted an association between post-traumatic stress and metabolic disorders. Based on the concept of Developmental Origins of Health and Diseases our study aimed to investigate whether early life stress can trigger metabolic disorders and associated key features i.e. low-grade inflammation and microbiota dysbiosis.

Maternal separation (MS) is an established model of early life stress in rodent. C3H/HeN mice pups were separated from their dam and the rest of the litter 3 hours per day during 10 days starting at post-natal day 2 (PND2). All experiments were carried out in male offspring aged of PND350 on standard diet. Metabolic state was evaluated by oral glucose tolerance test (OGTT) and intraperitoneal insulin tolerance test (ITT). Cellular immune response was analyzed by primary cell culture of spleen, *lamina propria* and mesenteric lymph nodes. Plasmatic and fecal Ig concentrations were measured by ELISA. Fecal microbiota composition was analyzed by GUT Low-Density Array (GULDA).

MS had no effect on body weight in male mice but increased fasted blood glycemia. Furthermore, MS induced glucose intolerance, measurable during OGTT. Blood glucose was higher at 15 min and 30 min in MS mice after oral administration of glucose. During ITT, blood glucose in MS mice diminished slower resulting in an increase of the area under the curve (blood glucose mg/dL/30min). MS did not affect cellular immune response. However, MS decreased IgG concentrations in plasma and feces without modification of IgA concentrations. Finally, MS induced fecal dysbiosis favoring pathobionts (*Bacteroides vulgatus*, *Enterobacteriaceae*, *Escherichia coli*, *Enterococcus spp*).

We demonstrated for the first time that early life stress induces glucose intolerance associated with a loss of insulin sensitivity in mice non-genetically predisposed to metabolic disorders and fed with standard diet. Interestingly, glucose intolerance is not associated with local or systemic low-grade inflammation but is associated with a decrease of humoral (IgG) response. Furthermore, MS induces a fecal dysbiosis favoring pathobionts.