
Press Release April 2, 2019: In 2007, the United Nations General Assembly unanimously declared 2 April as “World Autism Awareness Day” that is worldwide celebrated by various initiatives. In this occasion GEMMA project (which stands for Genome, Environment, Microbiome and Metabolome in Autism) releases its web site: www.gemma-project.eu

GEMMA is a project selected by the European Commission to identify treatment and prevention targets for autism spectrum disorders. GEMMA is a 5 year project that was kicked off on Jan 1st, 2019.

“We are in the midst of an epidemic of ASD, which parallels an increase in other chronic inflammatory disorders,” says Alessio Fasano, MD, director of the Ebris Foundation (Italy) and the Mucosal Immunology and Biology Research Center (MIBRC) and chief of the Division of Pediatric Gastroenterology and Nutrition at MassGeneral Hospital for children. "But the rate of growth is much steeper for ASD, with an increase from 1 in 5000 children in the mid-1970s to a staggering 1 in 59 in 2018."

According to a study from the London School of Economics, ASDs carry larger societal costs than cancer, heart disease and stroke combined. Fasano suspects that a variety of environmental factors might be helping to fuel this epidemic.

Researchers plan to enrol 600 infants at risk of developing ASD at centres in Italy, Ireland and the U.S. Infants will be followed very closely from birth, to monitor their progress toward the possible onset of ASD. Collecting stool, tissue and blood samples from children over a 5-year period - along with environmental data – scientists will study the interaction of the gut microbiota (microbe community) and its related mechanisms with the intestinal barrier and immune response. The goal of GEMMA is to identify biomarkers – measurable changes in the gut microbiota – that could predict development of ASD in genetically predisposed infants.

GEMMA participants include scientists from the European Biomedical Research Institute of Salerno, Nutricia Research, Medinok, Bio-Modeling Systems, Euformatics, Theoreo SRL, National University of Ireland Galway, Azienda Sanitaria Locale Salerno, Consiglio Nazionale delle Ricerche, Institut National de la Recherche Agronomique, the French National Institute of Health and Medical Research, Utrecht University, Tampere University, Imperial College London, John Hopkins University and Massachusetts General Hospital for Children. The consortium will employ experts in genomics, the microbiome, metabolomics, epidemiology, animal research models, clinical study design, biostatistics and artificial intelligence to build mathematical models to predict who will develop ASD. Total funding for the GEMMA project is €14.2 million. GEMMA is one of three projects selected for funding by the European Commission as part of its Horizon 2020 Programme.
Expectation

The year is 2025: Twelve-month old Gemma is at the doctor’s office accompanied by her mother and her 31 2-year old autistic brother. About a month ago, Gemma had been diagnosed with an otitis media that was successfully treated with a three-day course of a targeted oral antibiotic. Gemma’s mother reports that her otitis has been resolved, but that she now suffers from constipation and stomach-ache.

Gemma’s doctor can perform a set of recommended queries on Gemma’s whole genome sequencing, which is available for siblings of autistic children. The doctor knows that Gemma has a higher than average risk of expressing Autistic Spectrum Disorder (ASD). He orders a gut permeability test and an immune profiling of Gemma based on a blood sample, as well as a metagenomic, metatranscriptomic and metabolomic analysis based on a stool and urine sample. While the samples are analysed in search for biomarkers known to be predictors of ASD, a physical and behavioural examination on Gemma is conducted, showing satisfactory growth and all developmental milestones reached. By the end of the examination, the results of blood and stool analysis are complete. The results are worrying: they reveal that zonulin (a marker of enhanced gut permeability) appears to be elevated, that pro-inflammatory immune cells have been activated and that the gut microbiome appears unbalanced with low amounts of F. prausnitzii and a relatively high Enterobacteria count. The metatranscriptome results also suggest that the genes controlling lactate production by Lactobacilli have been downregulated, and the metabolomic analysis confirms a reduction of lactate in Gemma’s stools and an increase in urinary cresols. Based on the whole genome sequencing analysis and epigenetic changes, it is established that genes controlling an immune response have been activated. In fact, a PET scan of Gemma’s brain shows neuroinflammation. The doctor turns to his computer and performs a risk analysis using a set of multi-omic analysis algorithms for disease modelling, which reveal that the combination of Gemma’s positive biomarkers, immune profile, specific gene variants, gut microbiome and metabolome composition carries a 55-fold increased risk of developing ASD within 9 months. He prescribes administration of the probiotic Lactobacillus GG (LGG) at $10^{10}$ CFU/day for three months in order to re-establish proper microbiome composition and lactate production with the aim to prevent the onset of ASD.

The mother is stunned by the science behind this personalized preventive process and tells the doctor: «When we had our first child in 2018, autism was untreatable, and certainly not something that medicine could prevent.»

The doctor explains: «Medical science made a huge leap when researchers funded by a European research program called Horizon 2020 demonstrated the link between certain biomarkers and colonies in the intestinal microbiome causing the neuro-inflammation that could lead to autistic disorders. This led to restoring the gut balance with personalized probiotics, as an effective pathway to prevent autism, and this has been the single most important discovery in the field of autism to date.»
Three months later, Gemma is back in the doctor’s office. All stool and blood analyses revealing abnormal biomarkers are back to normal, and the PET scan of the brain is now normal. Gemma will enjoy a healthy, normal childhood. Meanwhile, Gemma’s brother also has been offered a new treatment that reduces the feedback mechanism between the body’s immune response mechanisms and some specific microbiome-derived biomarkers, acting through attenuation of the Toll-like receptor family of proteins.

About Bio-Modeling Systems (BMSystems):

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GEMMA PROGRAM

Interplay between environment, genome, epigenome, microbiome, metabolome, proteome, glycome and immune function

Biomarkers targeted by the pre-clinical and clinical studies