Developmental origins of non-communicable diseases and dysfunctions: Implications for animal production

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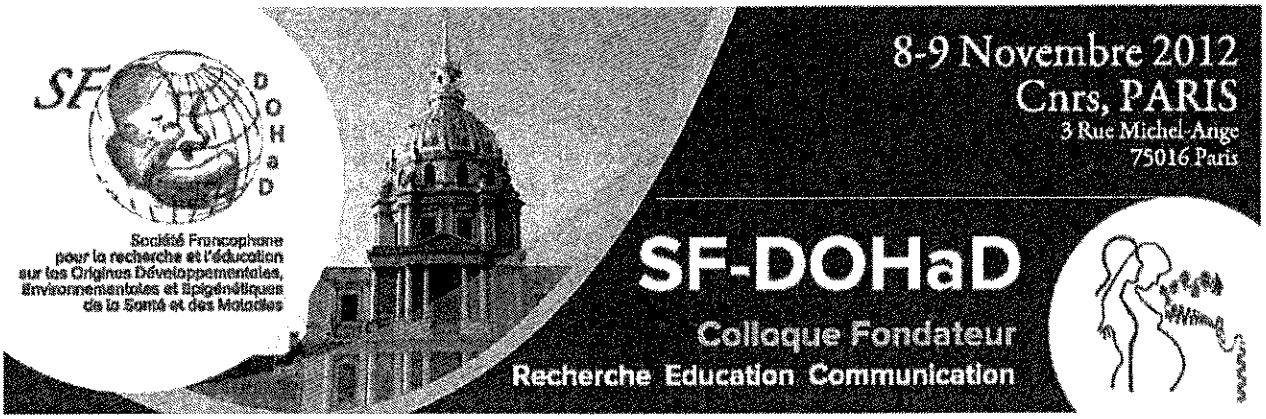

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Proceedings of the founding meeting of SF-DOHaD

STATE OF THE ART

1 – Developmental origins of health and disease: moving from biological concepts to interventions and policy

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The rising incidence of noncommunicable diseases (NCDs), especially in young adults, presents great humanitarian and economic challenges to high-resource and, increasingly, to low-resource countries. Noncommunicable diseases (NCDs), including cardiovascular disease, diabetes, chronic lung disease, allergy, some forms of cancer, cognitive decline, osteoporosis, sarcopenia, and affective disorders, are the world's biggest killers. Eighty percent of these deaths occur in low- and middle-income countries, especially as these countries undergo socioeconomic improvement after reductions in infectious disease. The World Health Organization predicts a global increase of 17% in NCDs over the next decade. No longer considered to be diseases of affluence, NCDs are exacerbated by urbanization and changes in social and lifestyle factors such as diet and family size. NCDs are preventable, but new initiatives are needed to institute such prevention, especially in early life. We emphasize that all children are affected by their early developmental conditions, not just children exposed to a very deficient environment, and that this has long-term consequences for their predisposition to NCDs. We highlight the biomedical implications of these developmental origins of health and disease (DOHaD) concept of NCDs and discuss the implications for health policy. New research emphasizes the importance of early life factors in establishing the risk of NCDs through inadequate responses to later challenges, such as an obesogenic environment. A new focus on interventions to promote a good start to life in at-risk populations necessitates revision of public health policy, with implications for the health, education, and empowerment of women and children in particular.

2 – Environmental Stressors in the Developmental Origins of Disease: Evidence and Mechanisms

Moshe Szyf

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A vast body of epidemiological data has suggested that childhood stress is associated with a variety of physical and mental health challenges later in life. The critical question is what is the mechanism? How could either physical- or social- stress early in life be registered in the genome of the offspring and stably affect the phenotype? We have been testing the hypothesis that DNA methylation, a covalent modification of the DNA, mediates the long term effects of early life environmental exposure on genome function.The pattern of distribution of methyl groups in DNA is different from cell-type to cell type and is conferring cell specific identity on DNA during cellular differentiation and organogenesis. This is an innate and highly programmed process. However, recent data suggests that DNA methylation is not only involved in cellular differentiation but that it is also involved in modulation of genome function in response to signals from the physical, biological and social environments. We propose that modulation of DNA methylation in response to environmental cues early in life serves as a mechanism of life-long genome "adaptation" that molecularly embeds the early experiences of a child ("nurture") in the genome ("nature"). Data that supports this hypothesis from rodent, non-human primates, humans and population studies will be discussed. We have established that the state of DNA methylation of a critical gene in physiological stress control, the glucocorticoid receptor is differentially methylated in adult humans hippocampus in association with early life adversity as it is in a rodent model of differential maternal care. We tested the hypothesis that the change in methylation that associates with early life adversity is not limited to several candidate genes but that it involves multiple functional gene networks and that it is not limited to the brain. We show differential DNA methylation landscapes in T-cells from rhesus monkeys that were deprived of a mother early in life as well as changes in DNA methylation in white blood cells from adults who were exposed to high social adversity early in life. Different early life experience are associated with different DNA methylation landscapes. These data support the hypothesis that exposure to stress early in life results in a broad genome-wide and system-wide change in the DNA methylation landscape that is hypothesized to serve as a genome adaptation mechanism.

3 – Developmental Origins of Non-Communicable Diseases and Dysfunctions: Implications for Animal production

Pascale Chavatte Palmer

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DOHAD mechanisms are shared by livestock. Worldwide, animal breeding activities play a major role in the reduction of poverty and the improvement of food security. We also currently face a growing need for animal products, to provide the necessary protein sources for human populations. Moreover, with the current global climatic changes, the breeding industry is required to adapt to the increasing incidence of biological hazards including

temperature rise, increasing risks and severity of draughts, river flood disasters and decreased crop yields. In terms of animal production, these fluctuations are likely to cause irregularity in the quantity of forage and cereal yield and to induce quantitative and qualitative variations in the diet provided to the animals with short or even long term periods of nutritional restriction. In animals raised for reproduction, these can result in long term physiological effects on animal health and reproductive parameters as well as on the quality and quantity of products. Through a better understanding of the effects and of the epigenetic mechanisms involved in DOHaD, in addition to the careful use of animal genetic selection, both animal production and welfare can be improved and some of the negative effects of feedstuff restriction could be prevented.

KEYNOTE SPEAKER

Neuroendocrine Origins of Obesity and Diabetes

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The incidence of obesity is increasing at an alarming rate and this worldwide epidemic represents an ominous predictor of increases in diseases such as type 2 diabetes and metabolic syndrome. Epidemiological and animals studies suggest that alteration of the metabolic and hormonal environment during critical periods of development is associated with increased risks for obesity, hypertension, and type 2 diabetes in later life. There is general recognition that the developing brain is more susceptible to environmental insults than the adult brain. In particular, there is growing appreciation that developmental programming of neuroendocrine systems by the perinatal environment represents a possible cause for these diseases. This talk will summarize the major stages of hypothalamic development and will discuss potential periods of vulnerability for the development of hypothalamic neurons involved in feeding regulation. It will also provide an overview of recent evidence concerning the action of perinatal hormones (including leptin and ghrelin) and nutrition in programming the development and organization of hypothalamic circuits that regulate energy balance and reproductive function.