MEDIA RELEASE

28 APRIL 2014

NATURE AND NURTURE: BABY’S DEVELOPMENT IS AFFECTED BY GENES AND CONDITIONS IN THE WOMB

A*STAR-led international study provides new insights into the relationship between genes and prenatal environment

A recent study led by A*STAR’s Singapore Institute for Clinical Sciences (SICS) found that genetics as well as the environment in the womb play important roles in the development of the baby. The effort by the international team of scientists and clinicians is the world’s first attempt to discover how genetic and environmental factors affect the human epigenome. The results have fundamental implications for how epigenetic studies will be conducted in the future and for our understanding of how the mother’s nutrition and lifestyle may have long-lasting effects on the health of her children.

In this study, samples of umbilical cord tissue were taken from 237 individuals in the GUSTO Birth Cohort Study and their epigenetic profiles were examined. While genetic differences alone accounted for 25% of epigenetic variation, up to 75% could be attributed to interaction between genetic differences and prenatal environments. This means that both prenatal and genetic factors closely related.

Earlier research has shown that some of prenatal factors such as maternal smoking, maternal depression, maternal weight, infant birth weight, gestational age and birth order affect the development of foetuses. This study shows that the most variable epigenetic marks among new-borns are most likely to be driven by a combination of genetic differences and the environment in which the baby develops before birth. Thus, future studies on human epigenetic variation could include an assessment of how much environmental influences are affected by

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1 Derived from the Greek, epigenome means “above” the genome. The epigenome consists of chemical compounds that modify, or mark, the genome in a way that tells it what to do, where to do it and when to do it. Although the marks are not part of the DNA itself, they can be passed on from cell to cell as cells divide, and from one generation to the next.
genetic differences. The findings were published in the respected genome biology and genomic medical journal *Genome Research*.

Coordinated by Senior Principal Investigator, Dr. Joanna Holbrook at A*STAR's SICS, and in collaboration with the Yong Loo Lin School of Medicine, National University Health System, KK Women's and Children's Hospital, and overseas partners in Canada, U.K., and New Zealand, samples from the GUSTO Birth Cohort Study (detailed in Annex A) were used for this landmark study on Asian epigenetics.

“The GUSTO birth cohort is an extremely powerful dataset to investigate how our experiences at the very beginnings of our lifetimes, in combination with our genes, affect our health throughout our lives. We see those messages transmitted via our DNA. We are asking fundamental questions about how the product of human evolution (our genes) interact with the individual circumstances we are born into, to shape our well-being,” remarked Dr Joanna Holbrook.

“These findings are likely to revolutionise our understanding of gene-environment interactions in early life and demonstrates the type of science that can be brought to bear when clinicians, basic scientists, and bio-informaticians work together,” said Associate Professor Chong Yap Seng, GUSTO Lead Investigator and Acting Executive Director at SICS.

Professor Keith Godfrey, Professor of Epidemiology and Human development at the Medical Research Council Lifecourse Epidemiology Unit, University of Southampton, iterated, “Epigenetics, and in particular DNA methylation marks, are thought to link a baby's development in the womb with its risk of obesity and heart disease in later life. This research provides important new evidence that fixed changes in a baby's genes have only a modest influence on its epigenetic profile at birth and that most of the variation between babies arises from interactions between the environment experienced in the womb and the genetic information inherited from the parents.”

Notes to Editor:

The research findings described in this media release can be found in the *Genome Research* Journal, under the title, “A*STAR Research Made Great Discoveries” by Ai Ling Teh*, Hong Pan*, Li Chen, Mei-Lyn Ong, Shaillay Dogra, Johnny Wong, Julia L Maclsaac, Sarah M Mah, Lisa M McEwen, Seang-Mei Saw, Keith M Godfrey, Yap-Seng Chong, Kenneth Kwek, Chee-Keong Kwoh, Shu-E Soh, Mary FF Chong, Sheila Barton, Neerja Karnani, Clara Y Cheong, Jan Paul Buschdorf, Walter Stunkel, Michael S Kobor, Michael J Meaney, Peter D Gluckman, Joanna D Holbrook.

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Annex A - About GUSTO Birth Cohort Study

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Full text of the paper can be accessed online from:
http://genome.cshlp.org/content/early/2014/04/07/gr.171439.113.full.pdf+html
About Singapore Institute for Clinical Sciences (SICS)

Established in 2007, the Singapore Institute for Clinical Sciences (SICS) is a research institute within the Agency for Science, Technology and Research (A*STAR), and its mission is to develop clinical and translational research programmes in key disease areas.

SICS is distinguished by its focus on clinical sciences and the use of innovative approaches and technologies that enable the efficient and effective study of human health and diseases. The clinical scientists in SICS conduct the full spectrum of “bench to bedside” research activities in metabolic diseases (including diabetes, obesity and insulin resistance), pathways to normal growth and development (including cognitive and behavioural development), and nutritional sciences. The institute aims to attract, train and nurture clinician-scientists and to develop joint programmes with universities, academic medical centres, government hospitals and research institutes.

For more information about SICS, visit www.sics.a-star.edu.sg.

About the Agency for Science, Technology and Research (A*STAR)

The Agency for Science, Technology and Research (A*STAR) is Singapore’s lead public sector agency that fosters world-class scientific research and talent to drive economic growth and transform Singapore into a vibrant knowledge-based and innovation driven economy.

In line with its mission-oriented mandate, A*STAR spearheads research and development in fields that are essential to growing Singapore’s manufacturing sector and catalysing new growth industries. A*STAR supports these economic clusters by providing intellectual, human and industrial capital to its partners in industry.

A*STAR oversees 18 biomedical sciences and physical sciences and engineering research entities, located in Biopolis and Fusionopolis, as well as their vicinity. These two R&D hubs house a bustling and diverse community of local and international research scientists and engineers from A*STAR’s research entities as well as a growing number of corporate laboratories.

For more information on A*STAR, please visit www.a-star.edu.sg.
ANNEX A - ABOUT GUSTO BIRTH COHORT STUDY

Incepted in 2009 as a collaborative effort with the two major public maternity hospitals in Singapore, National University Health System (NUHS) and the KK Women’s & Children’s Hospital (KKH), GUSTO is the region’s leading longitudinal birth cohort study that combines multi-ethnic Asian participants with detailed records of ante and post-natal data and biological specimens from both mother and child. These data include rare insights into newborn body composition and correlated future obesity via infant MRIs in the 1st week of birth, molecular analysis of birth tissues (placenta, umbilical cord, cord blood) and ongoing breast milk, stool, nasal and buccal swab specimens post-natal up to 2 years of age for the over 1200 mother-child pairs recruited. [Clinical/experimental] assessments include nutritional, biochemical, imaging, molecular and cognitive studies of the mothers and infants, with extensive implications for understanding future metabolic compromise, allergic and respiratory illnesses, cognitive spectrum childhood disorders and more. Additional information on the GUSTO study is available online at http://gusto.sg.