MEDIA RELEASE
EMBARGOED UNTIL 06 NOVEMBER 2015, 0800H SST

6 NOVEMBER 2015

SCRATCHING THE SURFACE OF SKIN DISEASE

Full genomic sequencing of all 14 species of the Malassezia genus opens up possibility of new treatments for microbially-mediated skin diseases

Singapore – An international team of scientists, led by researchers from A*STAR's Genome Institute of Singapore (GIS), Institute of Medical Biology (IMB), and Bioinformatics Institute (BII), and P&G, have completed the first comprehensive genomic and biologic study of all species of *Malassezia*, one of the top skin disease-causing microbes. The breakthrough study identified multiple potential targets for treating diseases such as seborrheic dermatitis, eczema and dandruff, all of which can be caused by *Malassezia*. *Malassezia* is also associated with skin cancer, the 6th most common cancer in males and the 7th in females in Singapore[1]. These findings improve our understanding of the human skin microbiome, with implications for dermatology and immunology. The study was published in the November issue of *PLOS Genetics*.

Malassezia is a type of yeast found on the skin of all birds and warm-blooded mammals, including humans. Often, *Malassezia* simply forms part of our normal skin flora, but for unknown reasons it sometimes causes disease. In particular, two species of *Malassezia*, *M. restricta* and *M. globosa*, are present on all human scalps and are responsible for common dandruff and seborrheic dermatitis[2]. Dandruff occurs when *Malassezia* feeds off fatty external lipids secreted naturally on the scalp, and the partially digested lipids lead to irritation. The link between dandruff and the two species was first discovered, and their genomes fully sequenced, by Dr Thomas Dawson and his team at P&G in 2007, which also developed subsequent hair care technologies to target them. However, much remained unknown about *Malassezia*.

By sequencing the genomes of all known *Malassezia*, (including multiple strains of those most common on human skin), the team identified hundreds of features explaining how the fungus may be able to thrive on human skin. The dependence

[1] 'Cancer Survival in Singapore, 1973-2012', Sep 2015, Singapore Cancer Registry, National Registry of Diseases Office, Ministry of Health, Singapore
[2] Seborrheic dermatitis is a common skin condition that mainly affects one's scalp. It causes scaly patches, red skin and stubborn dandruff.

of all *Malassezia* species on lipids for survival was also established, and the idea that they are sexually active remains supported. Through this knowledge, scientists can start finding ways to control their activity on human skin, and work towards the restoration of healthy skin.

Importantly, a gene unique to *Malassezia* and in no other related fungi, was also found. This gene is potentially the one which first allowed *Malassezia* to switch from living only on plants to being able to live on animals, birds and humans. In other words, by targeting this gene, we may be able to eliminate *Malassezia* on human skin, or weaken its growth and survival significantly. This discovery thus lays the groundwork for future work to develop therapeutics targeting the gene for a range of skin diseases.

The study is particularly relevant to Singapore and Southeast Asia, given that the hot and humid climate provides a perfect environment for fungi to thrive. In fact, Singapore has the highest reported incidence of fungal-mediated skin disease in the world[3], with about one in five people suffering from atopic dermatitis, or eczema[4]. Therapeutics and further research addressing *Malassezia* would therefore have widespread applications in the region.

Furthermore, scientists are increasingly turning to the human microbiome and the microorganisms living on humans for greater insight on human health. For example, the US National Institutes of Health (NIH) launched the Human Microbiome Project (HMP) in 2008 with a budget of US$115 million over five years[5]. *Malassezia* plays a dominant role in the human microbiome and knowing more about these fungi substantially improves our overall understanding. In particular, a database with the sequenced *Malassezia* genomes has been made public, allowing researchers worldwide to learn more about what was previously considered ‘dark matter’ on the skin.

Dr Thomas Dawson Jr., Senior Principal Investigator at A*STAR’s Institute of Medical Biology (IMB), principal author of the paper, and who previously led studies on *Malassezia* while at P&G, stated, “This new information will allow us to better understand healthy versus unhealthy skin and hopefully learn to modulate the skin microbiome so as to transform unhealthy into perfect, healthy skin.”

Dr Niranjan Nagarajan, Principal Investigator at A*STAR’s Genome Institute of Singapore (GIS) and co-author of the paper, said, “This study provides a comprehensive genetic resource for further investigations into Malassezia biology and its life on human skin. Particularly exciting was the identification of several genes horizontally acquired from bacteria that play an important role in making Malassezia unique.”

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[3] ‘The Global Burden of Skin Disease in 2010: An analysis of the Prevalence and Impact of Skin Conditions’, 2013, The Journal of Investigative Dermatology 134 (6), Nature Publishing Group
[4] ‘Eczema: All You Need to Know’, Health Xchange, SingHealth
[5] ‘NIH Launches Human Microbiome Project’, 19 Dec 2007, NIH Press Releases, NIH

Dr Benjamin Seet, Executive Director of A*STAR's Biomedical Research Council (BMRC), commented, "This study helps us understand how a microscopic organism that lives on the skin can give rise to a common disease like eczema that affects one in every five Singaporeans, as well as to serious conditions like skin cancer. Our partnership with P&G opens doors to important research that will benefit patients suffering from these conditions in Singapore, and which will otherwise not be conducted here."

Dr Jim Schwartz, P&G Research Fellow, observed, "Malassezia are at the centre of the incurable yet treatable conditions of dandruff and seborrheic dermatitis. The continued investment in understanding the fundamental nature of these organisms allows a more in-depth appreciation of how and why they trigger the annoying symptoms that reduce quality of life for those responsive to their metabolic activities. Being at the forefront of research in this field assures our therapeutic product technology will likewise represent state of the art efficacy now and in the future."

Notes to Editor:

The research findings described in this media release can be found in *PLOS Genetics*, under the title, "Genus-wide comparative genomics of *Malassezia* delineates its phylogeny, physiology, and niche adaptation on human skin", by Guangxi Wu*, He Zhao†, Chenhao Li*, Menaka Priyadarsani Rajapakse*, Wing Cheong Wong***, Jun Xu[††], Charles W. Saunders[††], Nancy L. Reeder[††], Raymond A. Reilman[††], Annika Scheynius[§], Sheng Sun**, Blake Robert Billmyre**, Wenjun Li[#], Anna Averette**, Piotr Mieczkowski[§§§], Joseph Heitman**, Bart Theelen[‡], Markus Schröder[§§], Paola Florez De Sessions*, Geraldine Butler[§§], Sebastian Maurer-Stroh***,†††, Teun Boekhout[‡], Niranjan Nagarajan*, Thomas L. Dawson, Jr. [##]

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As a Science and Technology Organisation, A*STAR bridges the gap between academia and industry. Our research creates economic growth and jobs for Singapore, and enhances lives by contributing to societal benefits such as improving outcomes in healthcare, urban living, and sustainability.

We play a key role in nurturing and developing a diversity of talent and leaders in our Agency and Research Institutes, the wider research community and industry. A*STAR oversees 18 biomedical sciences and physical sciences and engineering research entities primarily located in Biopolis and Fusionopolis.

For more information on A*STAR, please visit www.a-star.edu.sg.

About A*STAR's Bioinformatics Institute (BII)
The Bioinformatics Institute (BII) is an institute of the Agency for Science, Technology and Research (A*STAR). BII was set up in July 2001 as part of the national initiative to foster and advance biomedical research and human capital for a vibrant knowledge-based Singapore. With a multi-disciplinary focus and collaborative outlook, BII recognises the need for depth and breadth in all its activities for building a thriving world-class biomedical research, graduate training and development hub in Singapore. In addition, BII is proactively involved in

building a national resource centre in bioinformatics to meet the evolving needs of the scientific community in Singapore.

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About A*STAR's Genome Institute of Singapore (GIS)
The Genome Institute of Singapore (GIS) is an institute of the Agency for Science, Technology and Research (A*STAR). It has a global vision that seeks to use genomic sciences to achieve extraordinary improvements in human health and public prosperity. Established in 2000 as a centre for genomic discovery, the GIS will pursue the integration of technology, genetics and biology towards academic, economic and societal impact.

The key research areas at the GIS include Human Genetics, Infectious Diseases, Cancer Therapeutics and Stratified Oncology, Stem Cell and Regenerative Biology, Cancer Stem Cell Biology, Computational and Systems Biology, and Translational Research.

The genomics infrastructure at the GIS is utilised to train new scientific talent, to function as a bridge for academic and industrial research, and to explore scientific questions of high impact.

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About A*STAR's Institute of Medical Biology (IMB)
IMB is one of the Biomedical Sciences Institutes of the Agency for Science, Technology and Research (A*STAR). It was formed in 2007, with a mission to study mechanisms of human disease in order to discover new and effective therapeutic strategies for improved quality of life.

IMB has 20 research teams working in three primary focus areas - stem cells, genetic disease, and skin biology. The teams work closely with clinical collaborators as well as industry partners, to target the challenging interface between basic science and clinical medicine. IMB's strategic research topics are targeted at translational research to understand the mechanisms of human disease so as to identify new strategies for disease amelioration, cure and eradication and to improve health and wellbeing. Since 2011, IMB has also hosted the inter-research institute Skin Biology Cluster platform, and leads major strategic funding programs in rare genetic diseases and in skin biology. In 2013 IMB became a founding institute of the Skin Research Institute of Singapore.

For more information about IMB, please visit www.imb.a-star.edu.sg.

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