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ASX Release
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Second Ghent study demonstrates DOPlify™ suitability for liquid biopsy applications

Highlights

- Second University of Ghent study published demonstrating DOPlify™ is internationally competitive for cell-based liquid biopsy applications
- New results reinforce the earlier Ghent study published in July 2017 that DOPlify™ is a world leading Whole Genome Amplification kit

Adelaide, 11 December 2017: RHS Limited (ASX: RHS) ("RHS" or "the Company") is pleased to announce that the results from a second University of Ghent single cell Whole Genome Amplification (WGA) kit comparison have been published in Nature Scientific Reports, with the results confirming that RHS' DOPlify™ works robustly on cells prepared according to standard non-invasive prenatal or cancer testing protocols.

Patient blood samples are typically collected at collection centres and shipped to centralised laboratories for testing. In the case of liquid biopsies, this includes isolating and testing circulating fetal or cancer cells. Specialised blood collection tubes that limit degradation of the cells during shipping from the collection site to the laboratory are used. This is the first step for the broad uptake of personalised medicine, a revolution that is unfolding with improvements in genomic tools and analysis protocols. Once the cells are received by the laboratory, the DNA needs to be copied for testing, which is where DOPlify™ plays its pivotal role. Being able to accurately copy the DNA from these pre-treated cells is a prerequisite for the downstream analysis. The Ghent study compared the four best performing kits that they had selected based on their earlier benchmarking studies.

In the published new study, the University of Ghent researchers stored cells for 24 hours in Streck Cell-Free DNA BCT® tubes, which chemically treat the cells using a fixative that prevents cell lysis during shipping, then collected 1 cell or 3 cell samples. These samples were amplified with one of 4 single cell Whole Genome Amplification (WGA) kits; DOPlify™ (RHS Ltd), PicoPLEX® (Takara Bio, USA), Ampli1™ (Menarini Silicon Biosystems, Italy) or REPLI-g (Qiagen, Germany), after which the performance of each kit was compared.

As in the earlier publications by this research group, DOPlify™, PicoPLEX® and Ampli1™ all accurately detected deletions and duplications from whole chromosomes down to 3Mb, which is the most clinically-relevant measure of WGA kit performance for preimplantation screening and circulating tumour cell applications. The new information from this study is that these 3 kits performed just as well on fresh and treated cells. Conversely, the REPLI-g kit performed poorly and the results were unsuitable for determining copy number changes.

Additionally, this study included analysis of STR (Short Tandem Repeat) markers, which are used to detect maternal DNA contamination in prenatal screening. Both DOPlify™ and PicoPLEX® performed equally well on single cells. PicoPLEX® performed slightly better on the 3 cell samples. There were only 3 replicates for single cell and 3 cell inputs for each WGA kit, which significantly impacts the statistical outcomes of the testing. Additionally, RHS anticipates that using our proprietary target sequence enrichment protocol to specifically amplify the STR markers would improve the DOPlify™

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results. Again the Qiagen REPLI-g kit performed poorly, confirming that REPLI-g is the only kit of the 4 tested that is unsuitable to use in these applications on cells that have been chemically fixed and stored.

The authors pointed to one single cell sample that failed using PicoPLEX® and suggested that DOPlify™ and Ampli1™ are perhaps more robust and reproducible. DOPlify™ performed equally as well in this study on fixed cells and in the authors earlier study on fresh cells, confirming that cell fixing did not impact DOPlify™ performance. One of the considerations for the use of Ampli1™ is that the protocol takes almost 7 hours to complete, compared to less than 3 hours for DOPlify™ and PicoPLEX®. The authors concluded that PicoPLEX®, Ampli1™ and DOPlify™ all performed well and that the kit selected should be based on the intended downstream application. REPLI-g was noted by the authors as unsuitable for use on fixed cells.

RHS' CEO, Dr. Michelle Fraser, commented that "these external independent validations confirm the position and relevance of our products and expertise in rapidly emerging fields that are already transforming medicine. We are buoyed by these new results and look forward to seeing how DOPlify™ performs in more of these types of head-to-head kit comparisons. We are confident in the competitive advantages of DOPlify™ and see this publication as reinforcement of our product being one of a very small selection of highly performing single cell WGA kits available globally."

PicoPLEX® is currently the market leader for single cell whole genome amplification and is included in the Illumina VeriSeq product for PGT-A applications in IVF. Rubicon Genomics Inc, the developer of PicoPLEX® was acquired in December 2016 by Takara Bio USA for approximately USD\$75m. Ampli1™ is a product from Menarini-Silicon Biosystems, a subsidiary of the Menarini Group, which is a multinational pharmaceutical, biotechnology and diagnostics company headquartered in Italy. Ampli1™ was launched in 2012.

A copy of the publication is available at <https://www.nature.com/articles/s41598-017-17525-5.epdf>.

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About RHS

RHS is a developer of advanced single cell genomic technologies focussed on improving health and research outcomes, based on deep technical experience in the field. DOPlify™ is a platform product for whole genome amplification (WGA) of single or small numbers of cells. DOPlify™ is applicable to the global Next Generation Sequencing (NGS) market. PG-Seq™, RHS' NGS workflow and EmbryoCollect®, RHS' microarray workflow, both incorporate DOPlify™ and have been specifically designed for the genetic screening of IVF embryos.

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