Reproductive Health Science Ltd

At the forefront of single cell genetic analysis

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Dr Michelle Fraser, CEO and MD
22 November 2016

Forward Looking Statements

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Corporate Overview

Key assets

Intellectual property	• EmbryoCellect™ microarray granted patent family in all major territories • DOPlify™ trade secret and supplier exclusivity • DOPlify™ combined single gene enrichment; Provisional Patent pending
Primary value drivers	• Clinical impact in the IVF market • Significant technical advances and deep expertise in single cell genetic analysis • Global product sales and key partnerships

31 October 2016 data

ASX Code	RHS
Shares on Issue	79m
Share Price	7c
Options	6.1m*
Market Capitalisation	$5.5m
Cash at 31st October	$1.6m

* A further 6.8m options expire 31 Dec 2016

Recent Corporate Highlights

- DOPlify™ launched August 2016
- EmbryoCellect™ performance validation data released July 2016
- $1.5m capital raise completed October 2016

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ASX:RHS

- RHS has maintained a focus on being “At the forefront of single cell analysis”
- RHS has a state-of-the-art advanced single cell Whole Genome Amplification (WGA) product DOPlify™ that enables analysis by Next Generation Sequencing (NGS) &/or microarray workflows
- RHS has a foundation in our particular interest of improving IVF outcomes, with a proprietary robust microarray kit for Pre-implantation Genetic Screening (PGS) known as EmbryoCellect™ and capabilities for combined PGS & Pre-implantation Genetic Diagnosis (PGD) by NGS using DOPlify™

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RHS product pipeline

- DOPlify™ whole genome amplification kit was launched August 2016

  - Captures RHS' proprietary know-how for the lysis and Whole Genome Amplification (WGA) of single or small numbers of cells
  - Provides a solution for the amplification of limited DNA that enables analysis by a range of methods, including NGS (Next Generation Sequencing) &/or microarray pathways
  - Platform technology that can be used for a range of applications

- DOPlify™ is the first module of EmbryoCellect™, RHS' microarray kit for the IVF market

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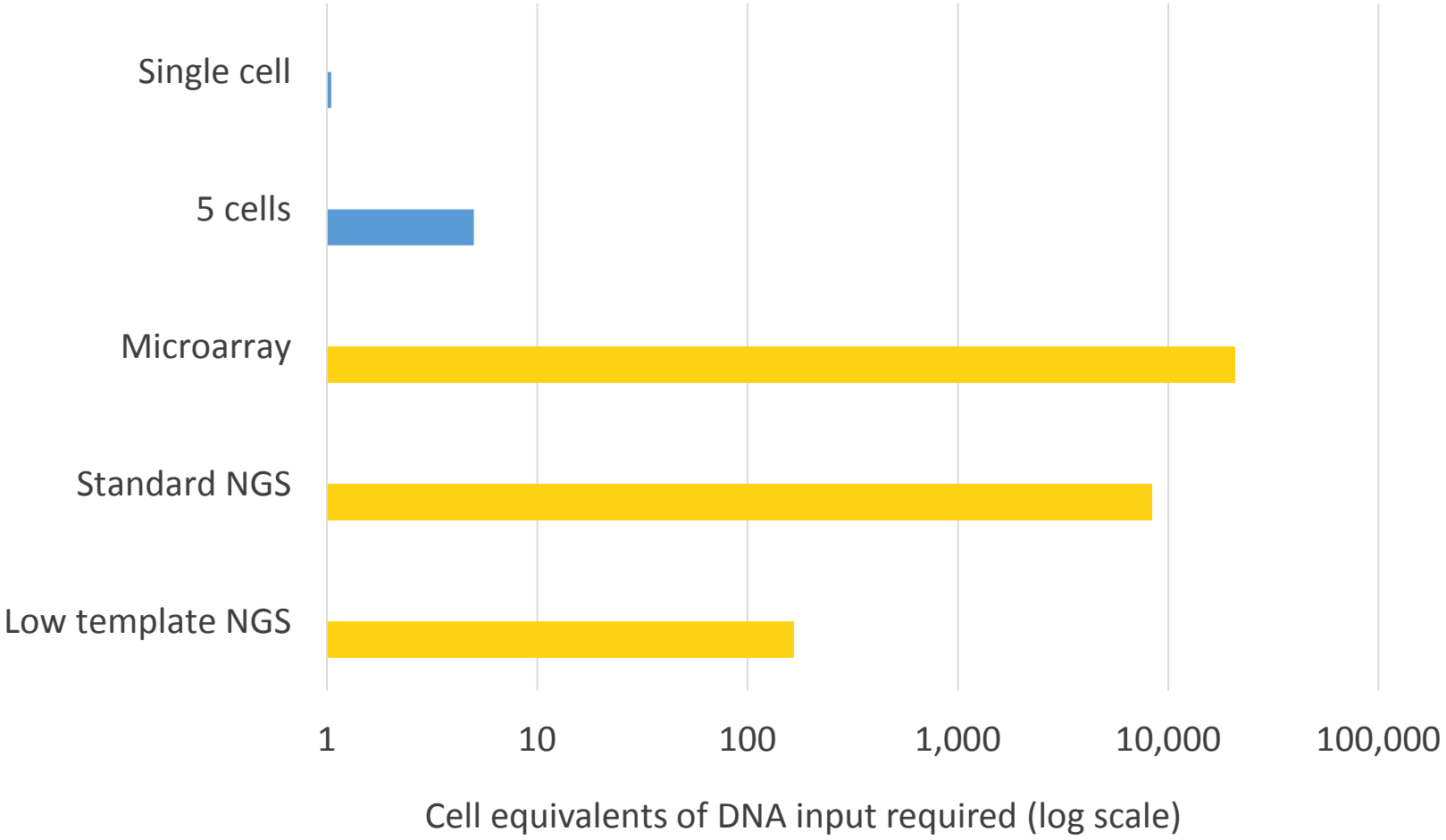
The need for Whole Genome Amplification



DOPlify™:
an enabling platform technology

- DOPlify™ is a solution to analyse “micro” quantities of DNA such as a single cell, which needs to be multiplied before analysis
- Analysis/interrogation of the DNA products of the amplification step can be by a range of approaches including NGS or array technologies
  - Accuracy of the subsequent DNA analysis is directly linked to the quality of the preceding WGA multiplication step
- The most advanced routine application of genetically analysing a single or small number of cells is in the IVF industry with embryo biopsies
  - This market provides a working model for other fields of single cell analysis

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DOPlify™ launch August 2016

- DOPlify™
  - contains one of only four approaches to WGA in the world (see Appendix Slide 23)
  - is unique in that it uses Advanced DOP-PCR, a modern version of a proven WGA approach
  - is a platform technology with significant competitive advantages and global applicability

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Competitive advantages of DOPlify™

- Simple protocol with only 2 sample tube openings
  - Minimises risk of contamination
  - Less steps than other WGA kits reducing hands on time
  - Clear QC prior to expensive downstream analysis
  - Fast protocol that matches the fastest on the market
- Latest generation reagents that are accurate and produce high yields of the DNA template
  - Robust kit shippable on ice packs and with a long shelf life
- Flexible WGA system that uniquely allows the addition of primers to copy specific regions of clinical significance concurrently (patent filed)
  - Targets include inherited disease causing genetic mutations, HLA-markers for donor matching
- Competitive genome coverage demonstrated by human mitochondrial genome data (see Appendix slide 25)

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The Opportunity for DOPlify™

- The single cell analysis market is forecast to reach US$3.35b by 2021 with a CAGR of 18.2% (http://www.marketsandmarkets.com/Market-Reports/single-cell-analysis-market-171955254.html)
  - Growth is predicted to mainly come from consumables, which is currently the largest segment
  - Instruments will also grow but their high cost and long shelf-life will be the limiting factor
- There is no further development required to use RHS' products across a range of applications, including IVF
- RHS is currently involved in a number of collaborations for IVF, cancer and other applications with results anticipated during the next few months

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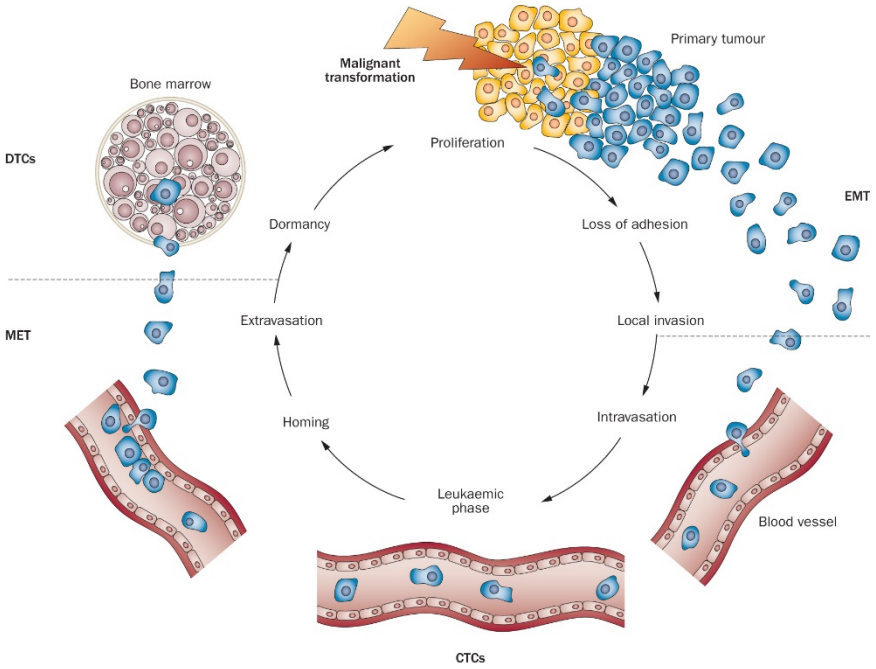
Single cell analysis in cancer



Permission obtained from Thieme © Schilling, D. et al. Mechanisms of tumour cell dissemination and methods for detection of circulating tumour cells in transitional cell carcinoma. Aktuelle Urol. 42, 122–127 (2011).

Schilling, D. *et al.* (2012) Isolated, disseminated and circulating tumour cells in prostate cancer *Nat. Rev. Urol.* doi:10.1038/nrurol.2012.136

Diversity within a tumour

- Growth characteristics
- Prediction of treatment response
- Metastatic potential

Detection and characterisation of circulating tumour cells

- Identification and prognosis of primary source
- Mutation rate compared to tumour
- Prediction and monitoring of treatment response
- Treatment effectiveness and recurrence

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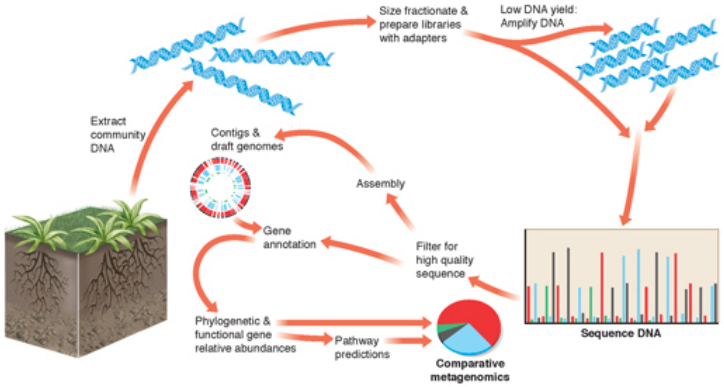
Research applications

Environmental DNA and conservation



MICROBE
Issue: July 2011, Dr. Jansson
Penumbra Design, Inc. 06/09/11
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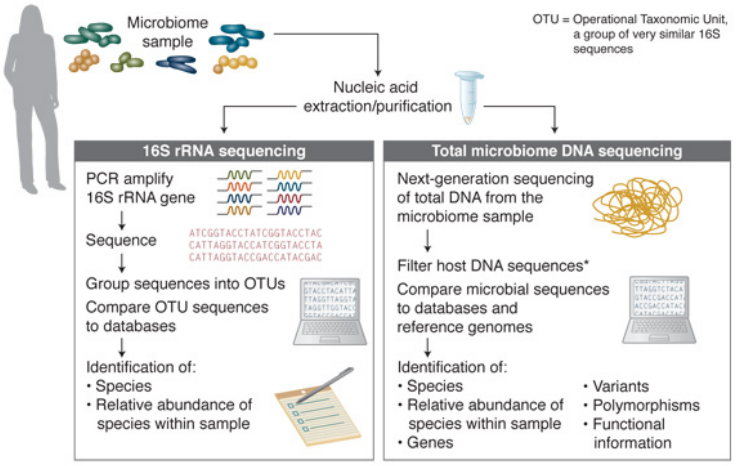
http://earthsciences.typepad.com/blog/2011/07/harnessing-metagenomics-to-study-microbial-ecology-in-soils.html

Human microbiome



https://www.neb.com/tools-and-resources/feature-articles/addressing-challenges-in-microbiome-dna-analysis

Using whole genome amplification, all of the DNA in a sample will be amplified, providing a more abundant template for analysis

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RHS products in IVF applications

- DOPlify™ DNA products from a single sample can be used for Next Generation Sequencing or microarray interrogation, providing choice and workflow flexibility
  - Targeted enrichment allows combined PGS and PGD
- The EmbryoCellect™ microarray PGS kit launched mid-2015
  - Designed specifically to meet the needs of the IVF industry
  - Developed and part-manufactured by RHS (this kit uses DOPlify™ as the first step for the microarray analysis)
  - Used to determine whether an embryo biopsy has the correct number of chromosomes

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Currently accessible PGS market

- There are 1.7 million IVF cycles per annum globally (2015 data), growing at 10%
  - An estimated 5 million IVF babies have been born, an average of one per classroom
  - RHS sells directly or has distributors in 45% of this market
- There are an average of 4 embryos per cycle, equating to 6.8m embryos per annum
- Over 1 million untested embryos are in frozen storage
- PGS rates vary by country, with an estimated 20% of Australian and 30% of USA IVF cycles using it
- RHS is focussed on increasing sales and services in Australasia, the USA and markets where distributors have been engaged

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RHS' PGS service opportunity

- The RHS PGS service was established to provide support to clinics introducing PGS
- The "Rollout" model is by direct services and supported sales;
  - flindersfertility is a functioning model of a clinic and RHS working together to determine the patient needs and specifically tailoring the testing, providing the option of fresh embryo transfer through fast turnaround analysis and the ability to identify euploid embryos prior to freezing
  - Morula IVF are an example of RHS assisting in the introduction and establishment of an in-house PGS capability through training, advice and technical support, which is now self-sufficient
- Broader roll out of this service model is anticipated both nationally and internationally
- Revenues from a PGS service business offered to 10,000 cycles in Australia (14% of the market) and assuming 30% PGS uptake in these cycles, approximates the total RHS operating costs

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Growth of the PGS market

- In the US, PGS is primarily offered by genetic testing service providers
- 2014 data indicated that less than 6% of IVF cycles in the US use PGS, but this has grown to 20% in 2016
- By 2020, RHS aims to be addressing 20% of the global PGS market, which is forecast to represent 20% of the global IVF market of approximately 2 million cycles
  - With an average of 4 embryos per cycle, this equates to 320,000 tests per annum in the IVF market

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RHS competitive advantages in IVF

- The RHS DOPlify™ WGA platform offers clinicians and their patients choice and flexibility for analysis of the precious embryo biopsy
  - Clinicians can determine on a patient-by-patient basis the extent of genetic information needed and tailor their screening accordingly
    - EmbryoCellect™ for cost efficient PGS, particularly under the time constraint for fresh transfer and to determine which embryos for frozen storage
    - NGS after DOPlify™ is ideally suited for PGD needs including translocations and specific inherited genetic disorders. It is possible to pre-determine clinically relevant regions to analyse when a couple carries an inherited disorder; hence RHS developed a unique and improved combined PGS-PGD approach

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Recent events

- RHS has released EmbryoCellect™ validation data showing the accuracy and sensitivity is competitive with claims of other PGS products
- A Patent application for combined PGS & PGD has been filed
- RHS launched DOPlify™ specifically targeting the NGS market and demonstrated a major, globally-unrivalled technical advance in being able to concurrently whole genome amplify and specifically amplify genes of clinical significance from single cells
- Flindersfertility co-located at Thebarton strengthening the connection with RHS and new IVF PGS/PGD service provision agreements commenced
- Consolidated and expanded the NGS capabilities of the Company including incorporation of this workflow into the PGS service business

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Revenue update
post October 4C and Quarterly review

- The initial reaction to DOPlify™ has been very positive with small volume sales and a number of collaborations with significant multinationals underway
- Delays in PGS service during Flindersfertility relocation appear resolved and RHS has expanded its PGS services and customer base
- Low base revenue is confidently expected to now build from this quarter, particularly with services revenues becoming more predictable
- Recently received the first $40K component of an Export Market Development Grant

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Focus for next 12 to 18 months

- RHS is actively marketing EmbryoCellect™ and DOPlify™ in USA market, a strategy that will be enhanced by strengthening the senior executive team and through RHS recently exhibiting at the American Society for Reproductive Medicine (ASRM) meeting in Salt Lake City in October 2016
- The launch of DOPlify™ is enhancing RHS' position as a global leader in single cell genomic technologies
- A number of significant opportunities are in progress due to our ability to respond to the advancing genetics market and to expand our focus to other important applications for single cell analysis. Commercial collaborations may lead to integration of DOPlify™ into the DNA analysis workflows of products of large multinationals
- With the margins achievable through product sales and services and with opportunities to access markets beyond IVF, RHS is focussed on becoming cash flow positive by the end of 2017

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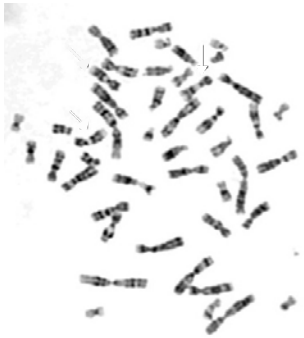
Appendix

What is Whole Genome Amplification?

cell

Lysis

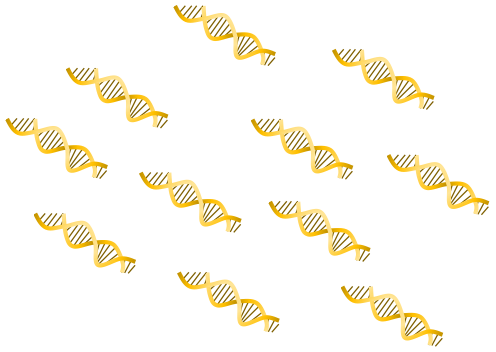
chromosomes



6 picograms of DNA

DNA

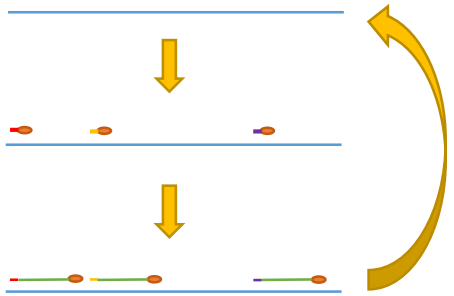
WGA



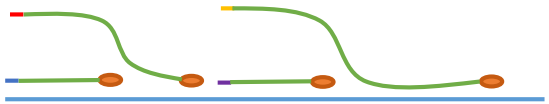
Whole Genome Amplification (WGA) copies the genome creating 1,000,000s of picograms of DNA from 1 cell

Commercially available WGA kits

- PCR-based WGA kits
  - Linker-adapter PCR (LA-PCR)
    - SurePlex (Illumina), PicoPlex (Rubicon Genomics), GenomePlex (Sigma)
    - *Ampli*1 (Silicon Biosystems)
  - Advanced DOP-PCR
    - DOPlify (RHS)



- Isothermal WGA kits
  - Multiple Displacement Amplification (MDA)
    - REPLI-g (Qiagen)
    - TruePrime (Sygnis)



- Hybrid WGA kits
  - LA-PCR + MDA
    - MALBAC (Yikon Genomics)
    - LIANTI

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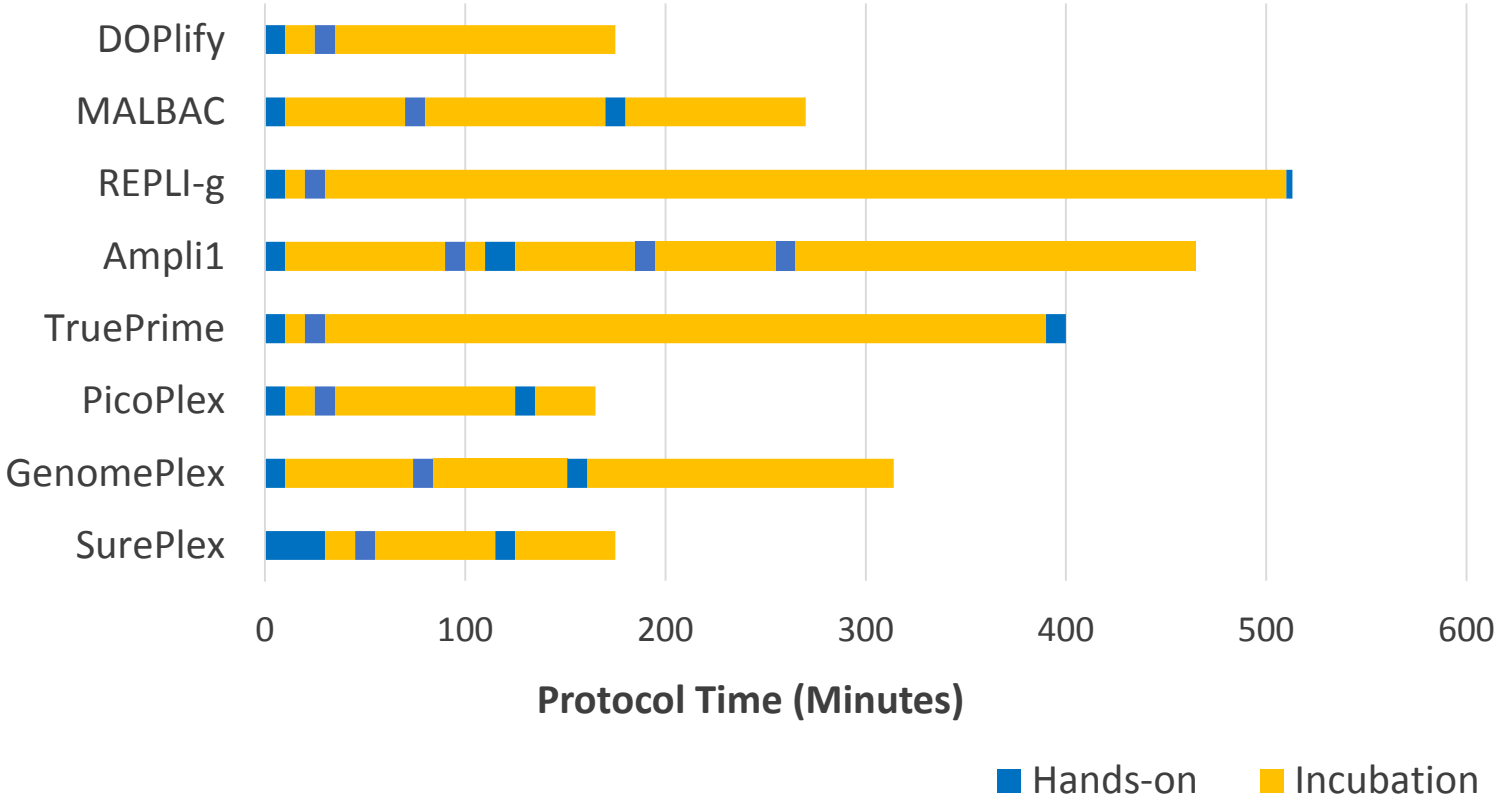
WGA protocol comparison



DOPlify™ is as fast as the fastest protocol and has less hands-on steps than any other single cell WGA kit, minimising the opportunity for sample contamination and providing a streamlined protocol

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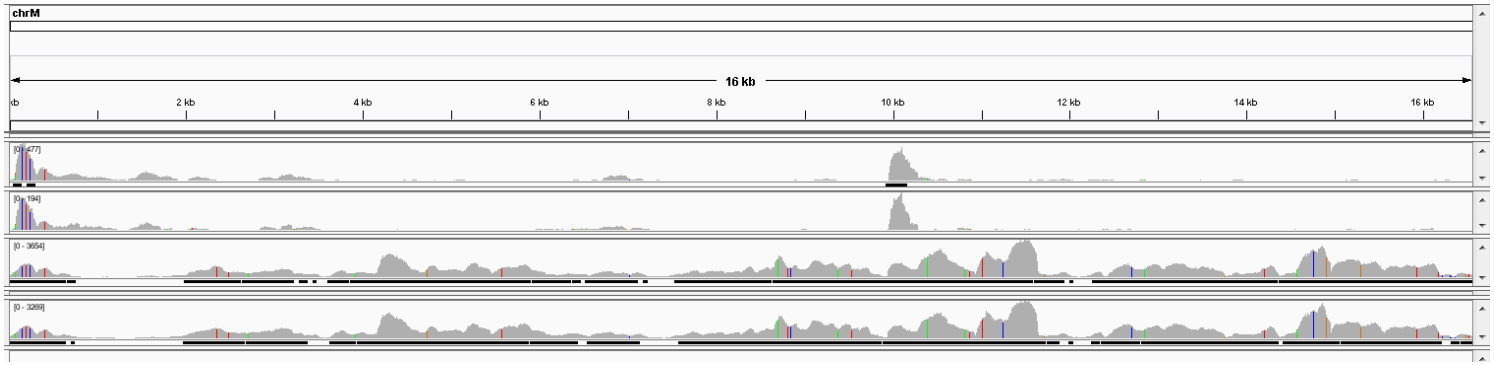
WGA benchmarking



Mitochondrial DNA sequence analysis of single cells amplified using either DOPlify™ or a competing WGA kit. Libraries were prepared using standard Nextera protocol and sequenced in the same 23-plex paired-end 150-bp read format on the Illumina NextSeq

- Identification of individuals can be achieved using mitochondrial DNA, which is maternally inherited, creating a target for forensics and genealogy
- Mutations in the mitochondrial genome have been linked to some diseases, including cancer, diabetes and deafness
- The number of mitochondria in an embryo has been associated with implantation potential and is being used in some clinics to rank euploid IVF embryos
- RHS internal benchmarking using single cells has shown that DOPlify™ provides greater coverage of the mitochondrial genome than a competing WGA kit

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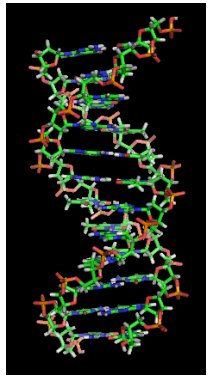
What is Next Generation Sequencing?

- DNA is made up of 4 bases, adenine (A), guanine (G), cytosine (C) and thymine (T)
- These bases make up the genetic code, determining the biology of a cell
- Sequencing is determining the genetic code of DNA. Once the code is determined, the fragment of DNA is matched and compared to a reference sequence



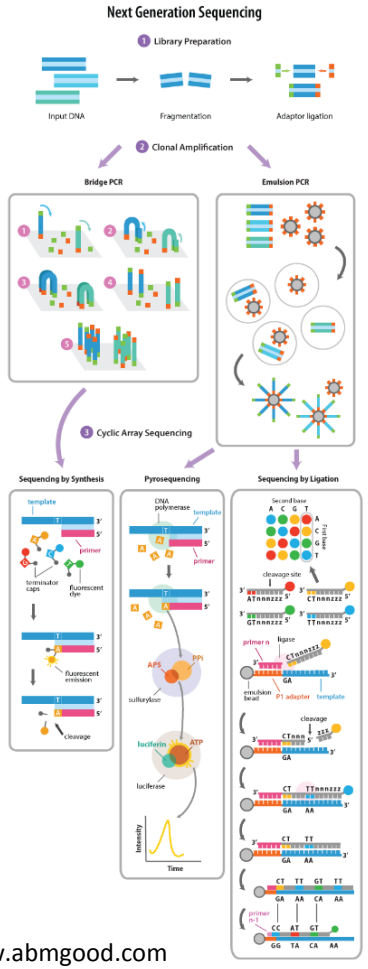
  - This can provide information on identity, genetic mutations and diseases, for example
  - Next Generation Sequencing (NGS), also known as massively parallel sequencing, is a method to sequencing millions of fragments of DNA at the same time. This increases throughput and brings down the cost

The Next Generation Sequencing workflow

DOPlify™ ⟶

Sequencing

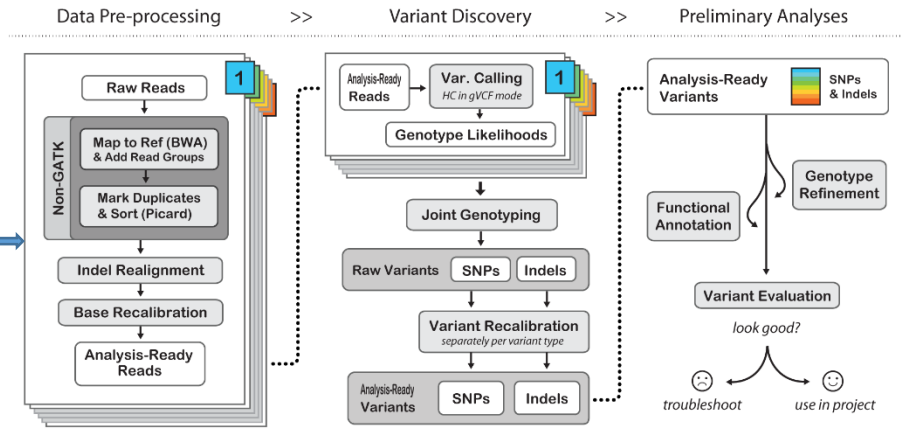
1. Library preparation
2. Determining the DNA code



www.abmgood.com

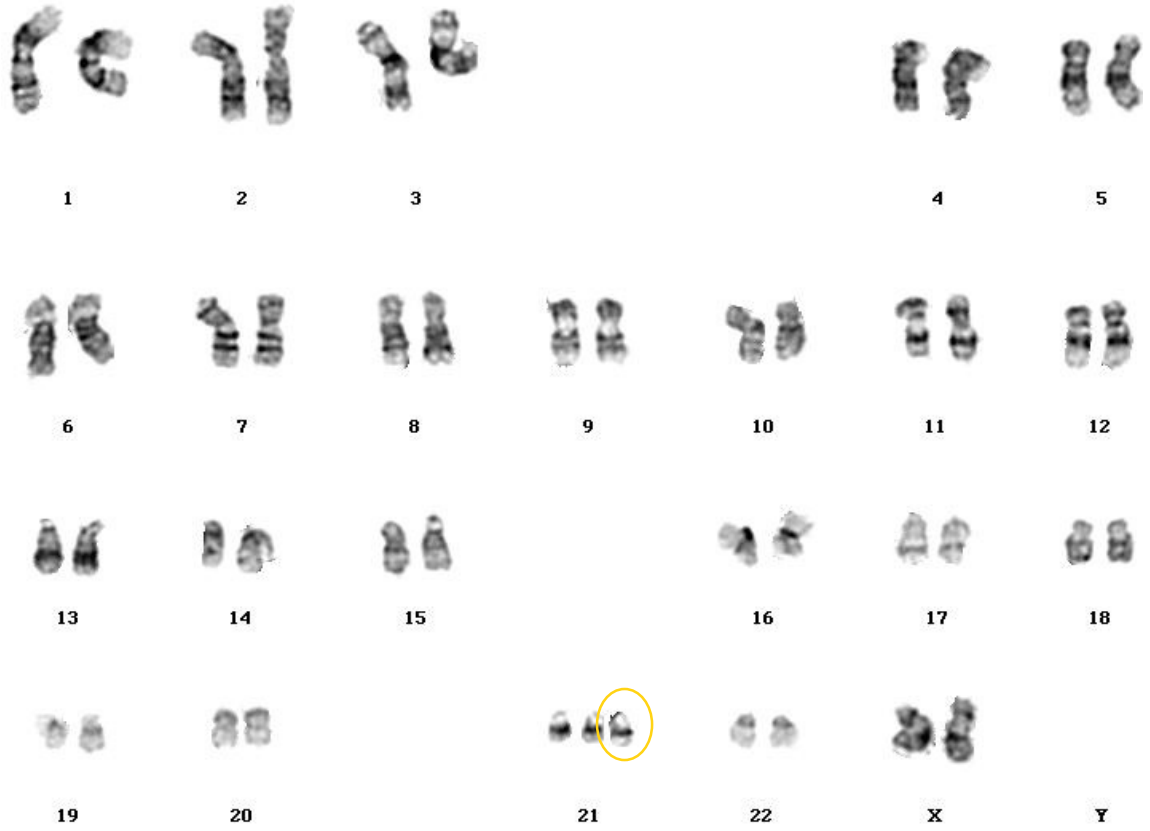
Bioinformatics

1. Checking the quality of the sequencing run
2. Working out where the >1million DNA fragments match within the entire human genome
3. Looking for differences with the reference genome
4. Determining whether the differences are clinically significant or not using published databases



http://www.broadinstitute.org/gatk/

Pre-implantation Genetic Screening



Euploid = correct number of chromosomes

Aneuploid = incorrect number of chromosomes

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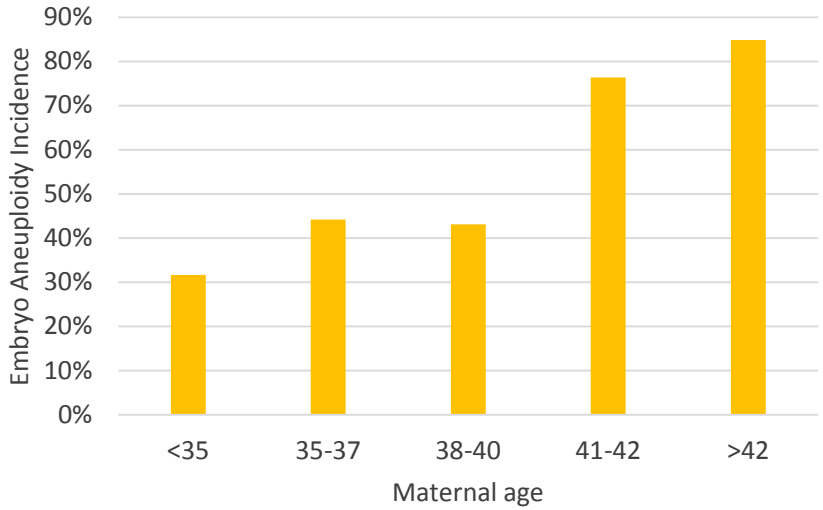
Aneuploidy and IVF outcome

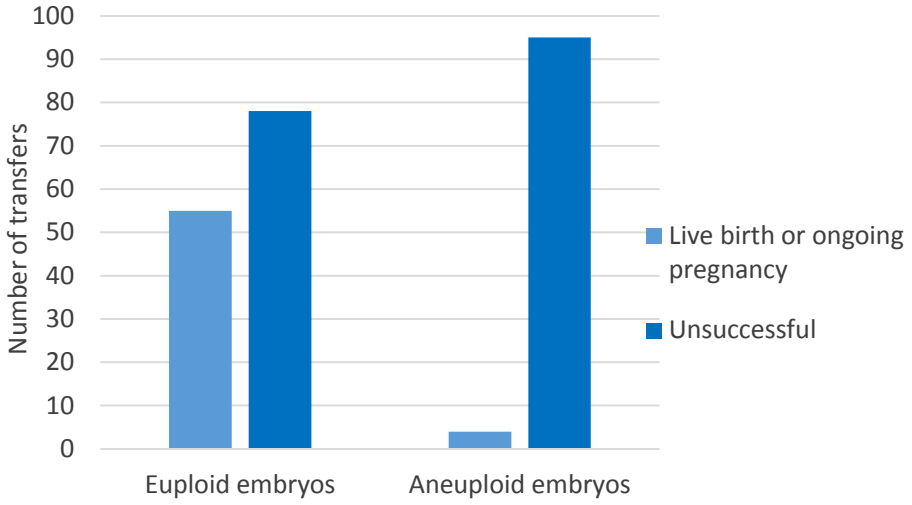


Even younger IVF patients have significant numbers of aneuploid embryos

Harton et al 2013

96% of the aneuploid embryos (ie embryos with the incorrect number of chromosomes) failed to implant resulting in an unsuccessful IVF transfer

Scott et al 2012



Influence of PGS on the IVF market

- Decreased time to pregnancy;
  - Transfer of a euploid embryo has been shown to overcome advanced maternal age factors
  - In some territories, family balancing is available
  - Decreased miscarriages
  - Increased single embryo transfers reducing clinical complications from multiple pregnancies eg preterm birth
- Patient and Medicare savings through efficiencies
- Clinic revenues impacted by reduced storage and subsequent transfer of aneuploid embryos but offset by additional revenues from PGS and repeat customers
- Patient expectations of best practice and clinical duty of care
  - Patients informed of their embryo status for planning & storage

Key Competitors in Single Cell Analysis

RHS product	Companies with competing technology
DOPlify™	Rubicon Genomics Inc, Sigma-Aldrich Co LLC, Qiagen NV, Yikon Genomics
EmbryoCellect™	Illumina Inc, Agilent Technologies Inc, Natera Inc, Oxford Gene Technologies
Next Generation Sequencing workflows	Illumina Inc, Fluidigm Corp, Thermo Fisher Scientific

RHS products compete across the DNA amplification, microarray and sequencing markets

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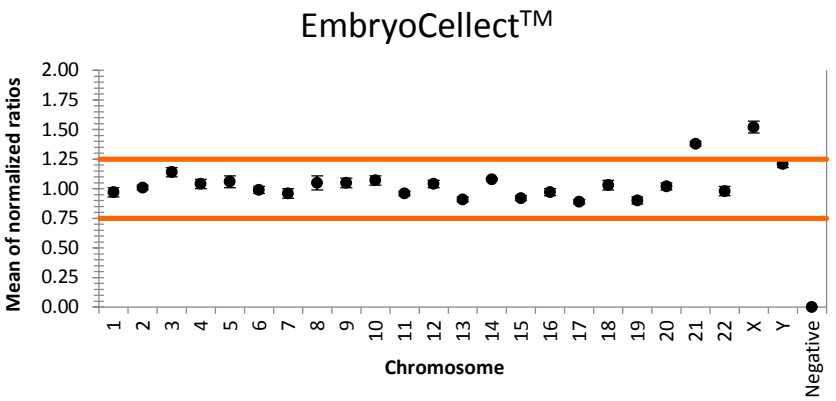
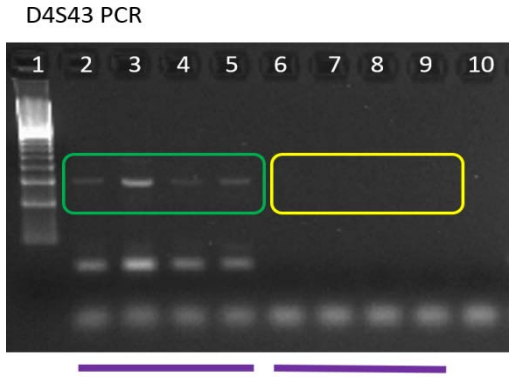
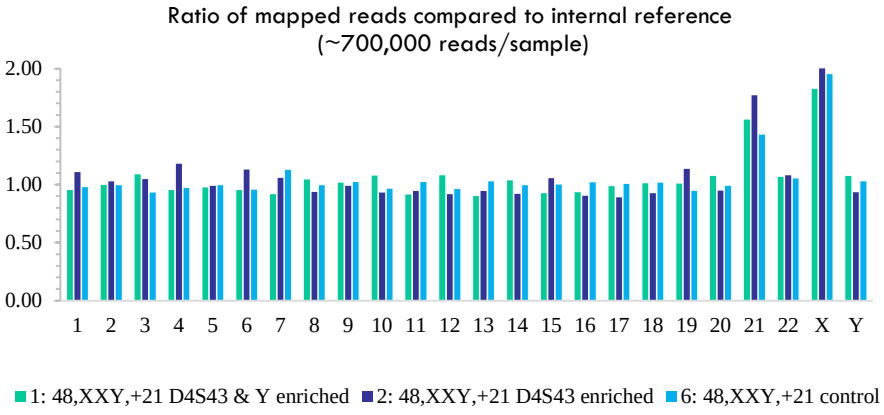
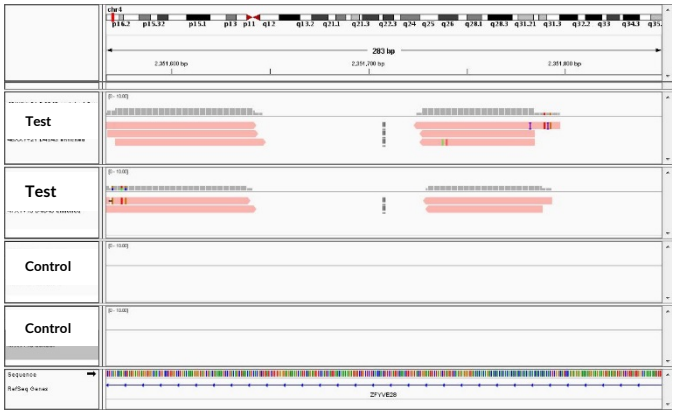
RHS combined PGS and PGD









Following DOPlify™ with targeted enrichment, the correct aneuploidy result is maintained and the targeted gene is analysable using traditional PGD and also NGS approaches. This is a unique approach with a patent filed

Board and Management

Dr David Brookes ***Non-Executive Chairman***	Director of Atcor Medical Holdings Ltd (ACG:ASX); medical practitioner & biotechnology consultant; MBBS; FACRRM; FAICD
Dr Michelle Fraser ***Managing Director and CEO***	PhD (molecular biology); Grad Dip Science & Technology Commercialisation; GAICD, RHS CEO since 2007
Ms Sue MacLeman ***Non-Executive Director***	CEO of MTPConnect; has been CEO and a Board member of a number of publicly-listed companies in both the USA and Australia; BPharm; MMktg; MLaw; FACPP; FAICD
Mr Johnathon Matthews ***Non-Executive Director***	General Manager of The Pipette Company; previously held positions at Australian Treasury, ASX and Commonwealth Bank; BEc; BComm; LLB; GAICD
Emeritus Professor Colin Matthews AO ***Alternate Non-Executive Director***	Inaugural director of RHS, Single Cell Pty Ltd, FlindersFertility; co-founder and former director of The Pipette Company; former Director ReproMed; Chairman RHS' Clinical & Scientific Advisory Committee
Mr Raymond Ridge ***CFO and Company Secretary***	CFO and Co Sec Thor Mining, CFO Southern Gold; BA (Acc); CA; GIA (Cert)
Dr Melinda Jasper ***CSO***	PhD; Experience in reproductive molecular biology, pre-implantation genetic analysis and single cell PCR, RHS CSO since 2012

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Reproductive Health Science Ltd ASX:RHS
Dr Michelle Fraser, CEO and MD
michelle.fraser@rhsc.com.au www.rhsc.com.au