NON-CONFIDENTIAL

OriCiro Genomics

Corporate presentation

April, 2019

OriCiro

Version 07

Contents

1. Company

- **Founded in December 2018, located in Tokyo**
- **People**

  Seiji Hirasaki, CEO

  Masayuki Su'etsugu, Ph.D., CSO, Associate Professor, Rikkyo University
- **Series A closed in March 2019 ($3.6M from UTEC)**
- **Mission: to create a better Bioeconomy with innovative genome technologies**
- **Focused on cell-free synthesis and amplification of large DNA (~1Mbp)**

Problem: Cell-based DNA cloning has been the gold standard for a while...

1973 Cohen and Boyer

2019

1973 Cooper and Mitchell

Wikimedia Commons

2019

by rawpixel on Unsplash

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Solution: Cell-free amplification of large DNA replacing cell-based cloning

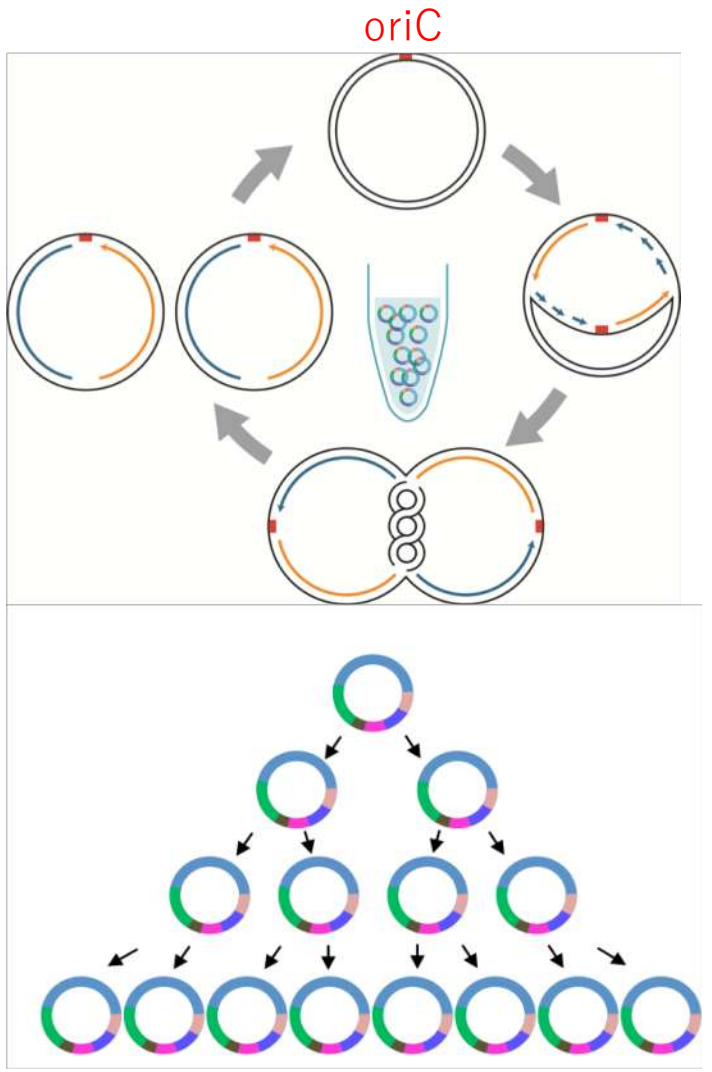
- Rapid amplification method reducing the required time to 1/10 of E. coli cloning
- Streamlines the research process, simple and easy-to-handle
- Widens the scope of existing research and development, allowing for amplification of previously infeasible sequences such as GC rich, repeat and cell toxicity-inducing sequences
- Unlocks the possibility of synthetic biology

2. Technology

1. Cell-free amplification of large DNA
2. Cell-free assembly of DNA fragments

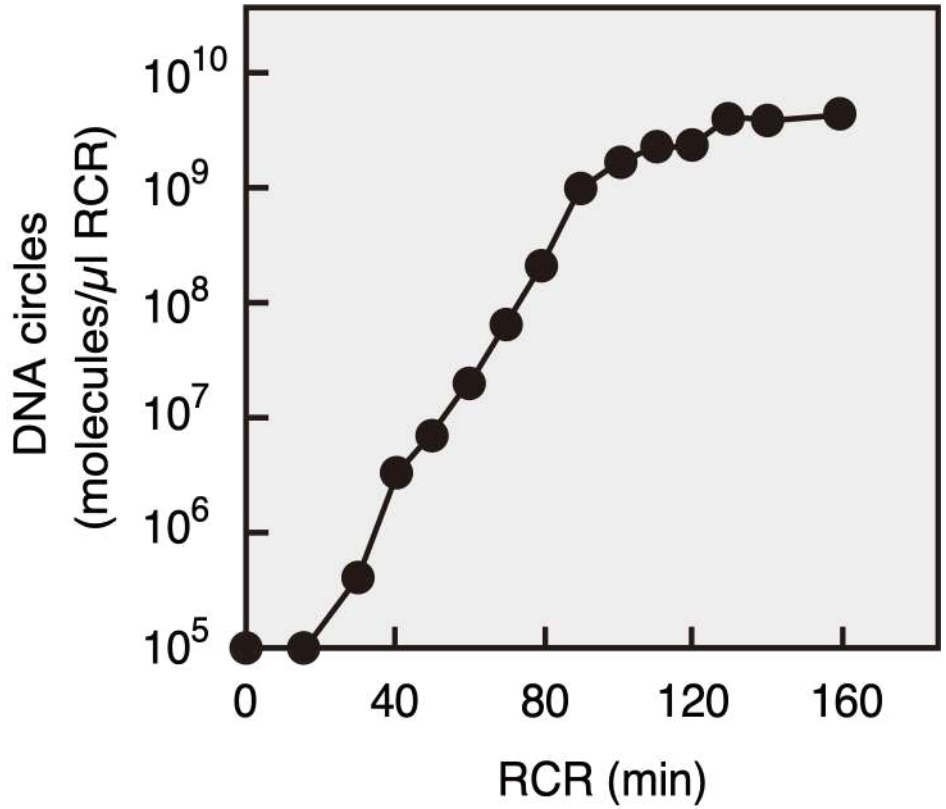
Reconstructing the E. coli genome propagation process in vitro

- Identified 25 proteins essential for E. coli genome propagation and reconstructed the entire propagation process in vitro
- Isothermal incubation at 30℃ for several hours
- Amplification in an exponential manner
- Self-sustaining and repetitive replication process
- Only requirement: circular DNA having *oriC* sequence (0.3kbp)



Outstanding performance of amplification by simple process

- ~10^{10}-fold amplification from a single DNA molecule within 3 hours at 30℃ (10 kbp DNA)
- Cell-free, easy-to-handle process
- Applicable to large circular DNA up to 1Mbp
- Applicable to any sequence (no restrictions)
- No recombinant DNA experiment



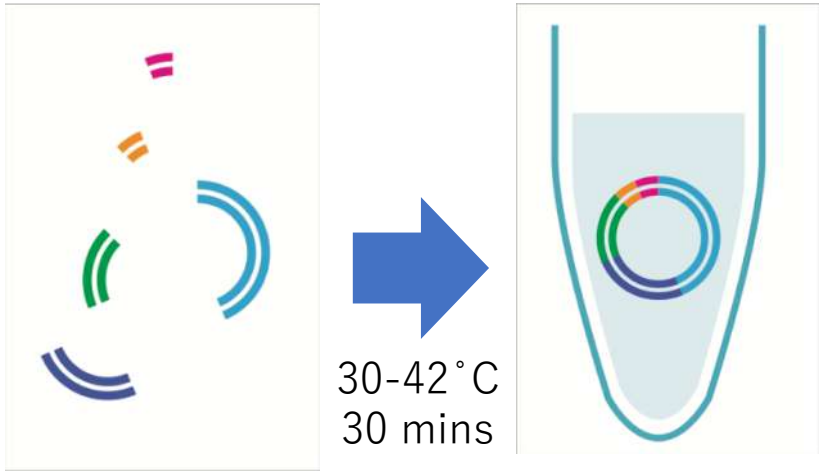
Nucleic Acids Research, 2017, Vol 45, No. 20 11525-11534

Distinctive Advantages

	PCR	E. coli cloning	OriCiro Technology
DNA size	+ (<10kbp)	++ (<300kbp)	+++ (<1Mbp)
Operation	Thermal cycling instruments	Cumbersome process Several days requiring techniques	Very simple process Several hours of isothermal incubation
Biosafety	Cell-free	Recombinant DNA experiment	Cell-free
Fidelity	+ (10^{-4}~10^{-6} error/bp)	+++ (10^{-10} error/bp)	++ (10^{-8} error/bp)
Sequence applicability	Not applicable to GC rich and repeat sequences	Not applicable to sequences that cause cell toxicity	Applicable to any sequence
Product	Linear DNA	Circular DNA	Circular DNA

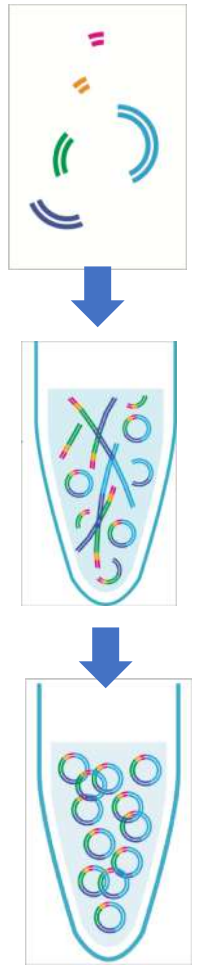
Assembly technology

- One-step assembly of multiple DNA fragments using homologous sequences of the fragment ends
- Simultaneous assembly of up to 50 fragments
- Enzymatic reaction
- No thermal cycling required



Assembly+Amplification: Efficient synthesis of genome-size DNA

- **Synergetic effect by combining assembly and amplification processes**
- **Unnecessary (linear) DNA is “shaken off” because only circular DNA is amplified**
- **No need of purification unlike in E. coli cloning**
- **Enabling cell-free synthesis of genome-size DNA**



IP: Covering broad area of applications with long patent life

	Application/ Publication No.	Expires	Countries	Status
Amplification	WO2016080424	2035	US, EP, JP, CN	JP: Granted (626287) US: Notice of Allowance issued EP, CN: Under review
	WO2017199991	2037	US, EP, JP, AU, CA, CN, IL, IN, KR, RU, SG	National phase
	WO2018159669	2038	WIPO	PCT application filed
Assembly	WO2019009361	2038	WIPO	PCT application filed
Editing	2018-142274	2038	JP	PCT application to be filed yet-to-be published

3. Wide range of potential applications

- Any research process currently using E. coli cloning
- Plasmid DNA manufacturing
- Modifications of microbe genomes
- Sample preparation for the next generation sequencing
- Building artificial genomes from DNA oligos
- New approaches to genetic diagnosis and gene therapy
- DNA data storage
- DNA as an advanced material

4. Products and Services

- Reagent kits for large DNA amplification and assembly for academia research
- Technology licensing to CDMOs for plasmid DNA manufacturing
- Custom-made libraries of large DNA
- Co-development

5. Future partnership

- Distribution of the reagent kits
- Plasmid DNA manufacturing (CDMOs)
- Co-development based on our proprietary technology
- Investors for Series B financing

Summary

- OriCiro offers cutting-edge, cell-free technologies for large DNA synthesis and amplification
- Increases the efficiency and widens the scope of partners' R&D dramatically
- Unlocks the potential of synthetic biology
- Seeks partnership opportunities

Contact

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