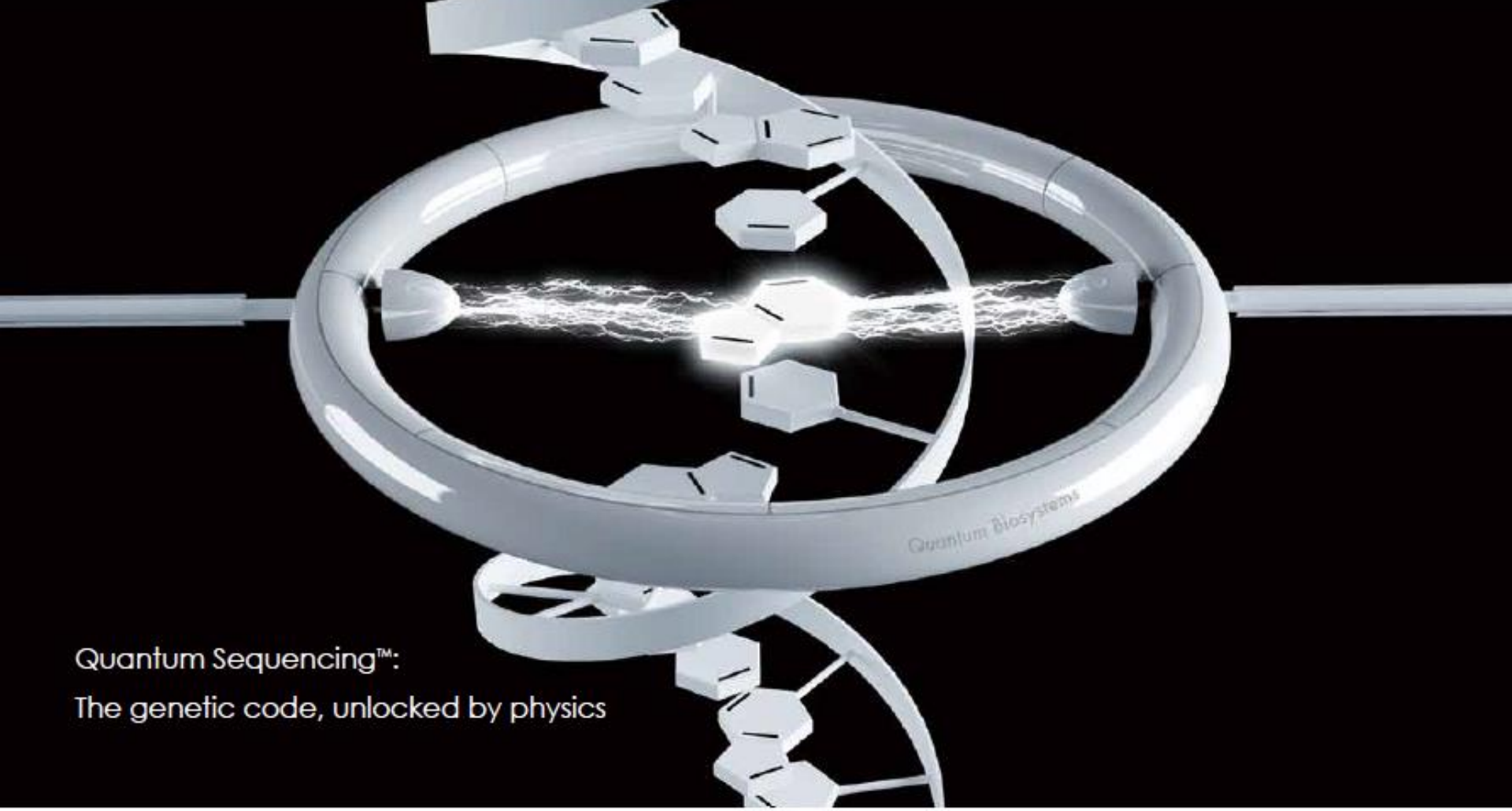


Innovation Seminar Series “Bridging science and business”

21 July 2017 | OIST Graduate University | Okinawa, Japan

Topics

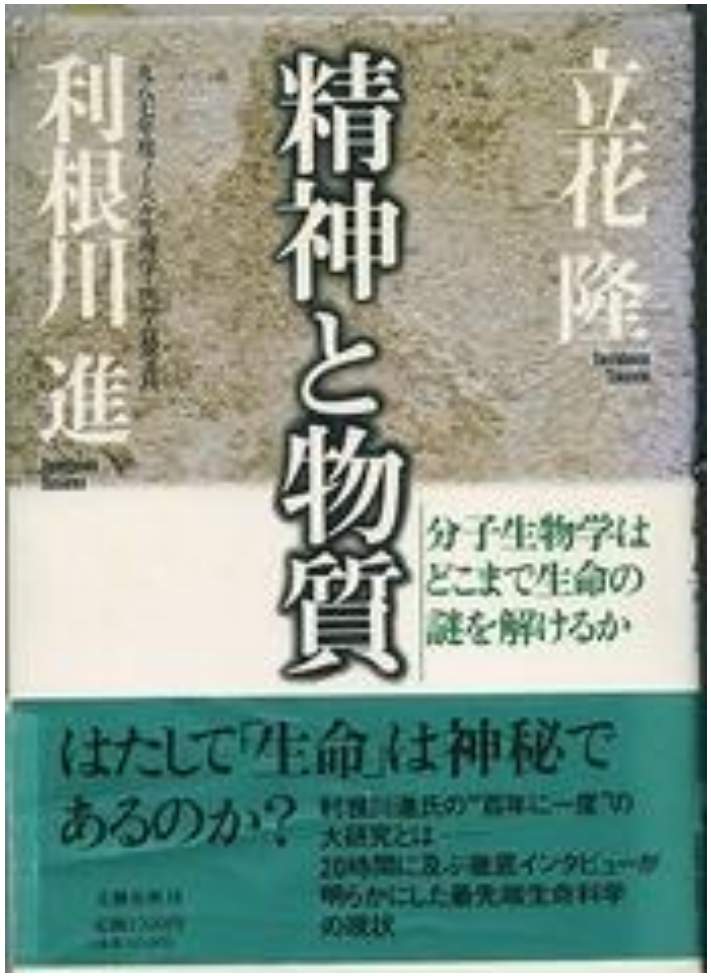
- **Who I am?**
  Self introduction

- What we do ?
  Disruptive innovation through DNA sequencer

- How we set up a start-up ?
  Technology seed from Osaka Univ

- How we made it global start-up ?
  R&D by “One Team” across countries

The most exciting and epoch-making breakthrough in this century would be driven by innovative biotechnology



Takashi Tachibana and Susume Tonegawa
「精神と物質」 文芸春秋 1990

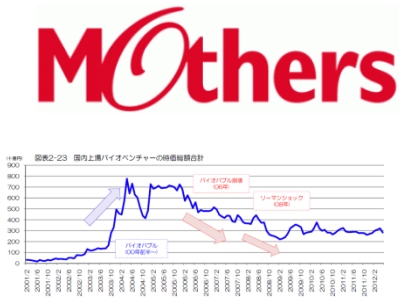
「精神と物質」を読んで高校時代に進路を決定

大航海時代に生まれていたら、僕は船乗りになっていたと思う。時代には、その時々で最もチャレンジングな領域がある。どんな時代でも、その最前線に身を置きたい。100年に一度という革新的イベントの一端に参加していたい。だから僕はバイオを選んだ。「ヒトってなに？」哲学や宗教に委ねていた問題を、サイエンスで解き明かしたい。不治と言われる病息も治療法は存在するはず、それは心底ワクワクする分野だった。

（McKinsey & Company　リクルーティング冊子より抜粋）

Source: QB

My career path - mainly focused on Biotech industry - but from various business facets

	Research associate (Tokyo Univ)	Equity research analyst (Shinko/Mizuho)	Management Consultant (McKinsey & Co)	Investment fund (INCJ)
Year	2001～2002	2003～2005	2005～2011 （2009 Columbia MBA）	2011～2012
Career	Human genome analysis with bioinformatics approach	Analyzing business and company values of biotech/ phramcos	Developing strategy for mega-pharmacos/healthcare companies (R&D, operation, marketing and org)	Investing life science and/or biotech start-ups and its post investments management
Key events				
	Completion of Human genome project	Biotech IPO bubbles	Inefficiency in R&D Generics penetration Frequent big M&A	Regenerative medicine and emerging technologies

Source: QB

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Next generation sequencing as “Disruptive innovation”: QB’s target is to realize a disruptive “$100, 1 hour” sequencer

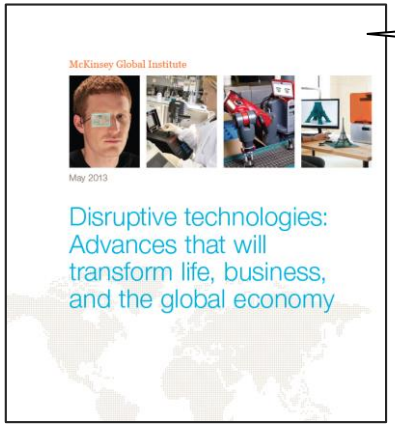
Impact of next generation DNA sequencing*

$2.7 billion, 13 years

Cost and duration of the Human Genome Project, complete in 2003

$100, 1 hour

Cost and time to sequence a human genome in the next decade



“We estimate that next-generation genomics have a **potential economic impact of $700 billion to $1.6 trillion per year by 2025**”

“**The impact of disease prevention and treatment applications** that we address could **be $500 billion to $1.2 trillion per year in 2025**”

“New technology has the potential **to improve treatment of genetically linked diseases** such as cancer and cardiovascular diseases, which currently kill around 26 million patients per year”

source: McKinsey Global Institute: Disruptive technologies , May 2013

The impact of realizing an innovative DNA sequencer will be beyond clinical and healthcare applications

QB's mission

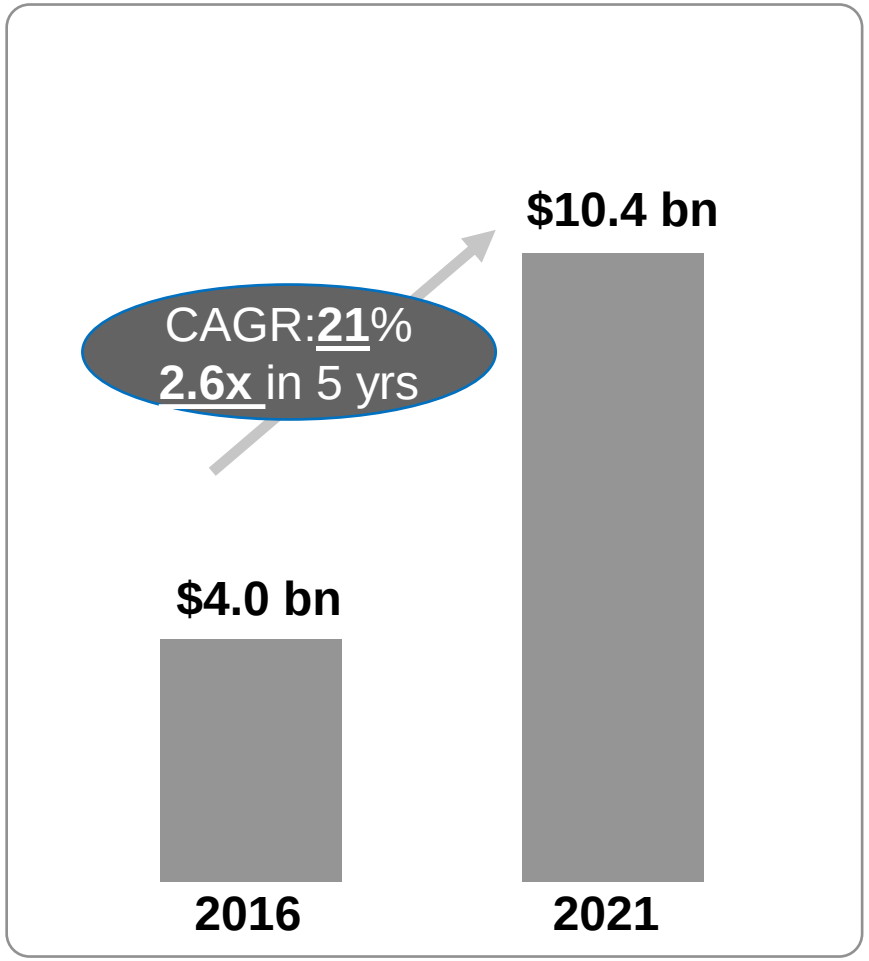
"QBs' mission is to unlock the vast untapped value of genetic information through the development of innovative sequencers."

- All living things on the earth have their unique DNA and deciphering its information helps solving global challenges such as healthcare, food and environmental problems
- However, its value is locked in its DNA chemicals which need to be converted into digital information – That's the DNA sequencer. Unlock the value of genetic information

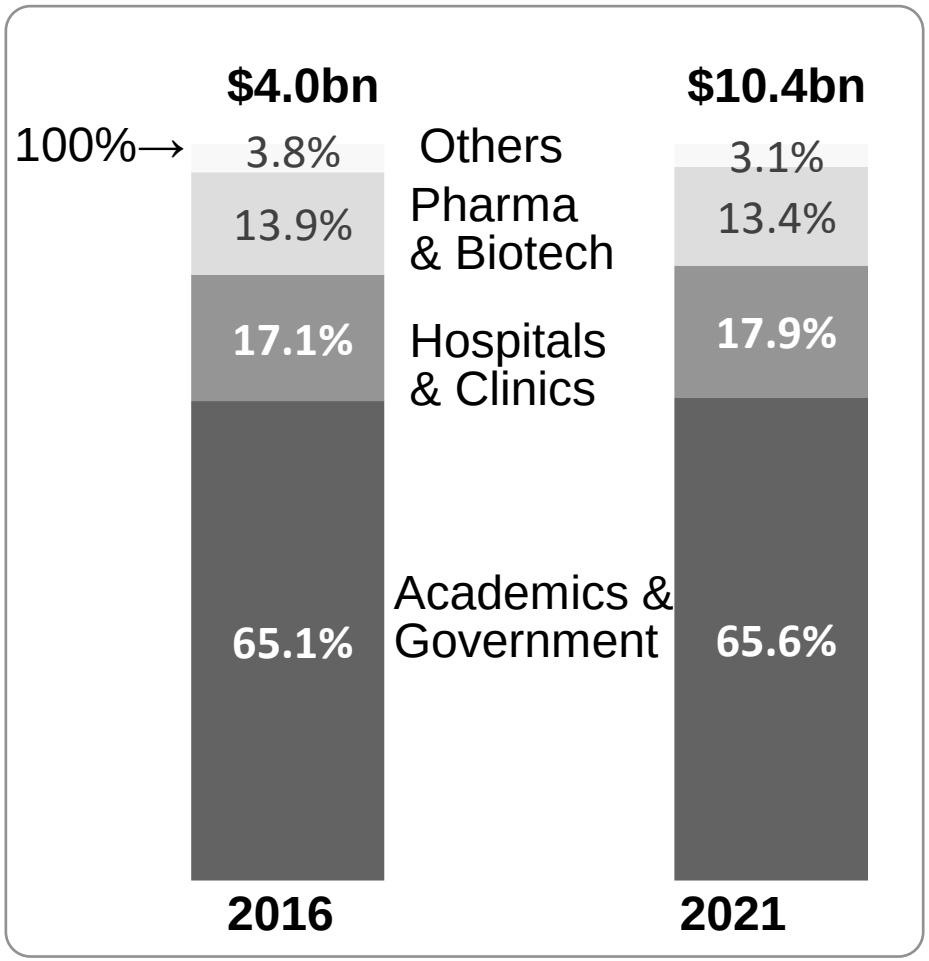
Source: QB

Market will be continuously expanded and clinical applications can become the major driver for growth

Global NGS Market, $bn



Market by Segment, $bn

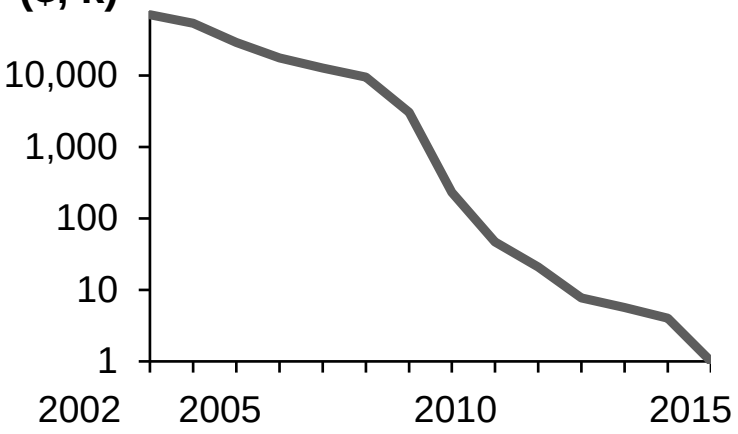


Clinical applications could become 50-80% after 2020 based on multiple reports and interviews. Key driver is whether low cost "clinical grade" NGS becomes available.

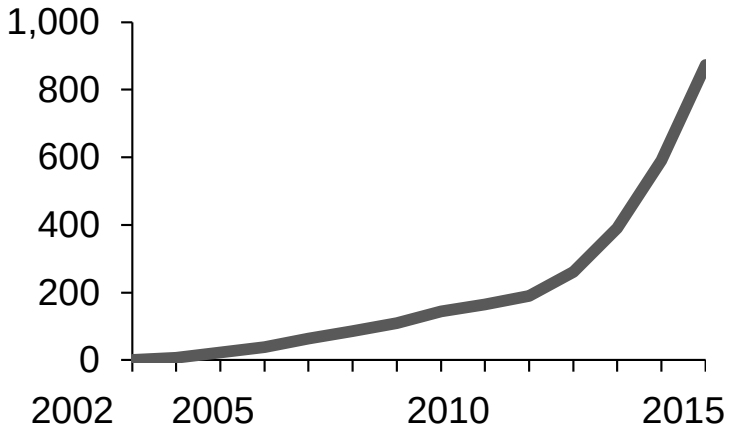
Source: BCC Market report, Markets & Markets NGS report

Recognizing the “big data” opportunities, High-Tech giants are already entering the market

Human genome sequencing cost ($, k)



Sequenced data (WGS) at Genbank (bp, bn)



High-tech giants movement

- Google started creating world’s largest human genome database.
  - To create a complete picture of a healthy human genome
  - To identify biomarkers for early detection of diseases

- Started collaboration with researchers to launch apps allowing iPhone owners to test their DNA
- The apps are based on “Research Kit” platform, recently introduced by Apple

- IBM's cloud-based Watson for Genomics started its service to 10,000 American veterans diagnosed with cancer over the next two years.

Source: Computational Technology Development Broad Institute of MIT and Harvard

Latest trends in big initiatives and big players' moves: showing more opportunities for accurate and inexpensive NGS

Recent news

Government driven initiatives

- 100,000 genomes project by UK government to sequence 100k genomes from around 70k people with a rare disease including cancer for genomic research – *100,000 genomes project*
- Precision Medicine initiative by Obama: Gather genomic data from consumers to discover new treatments tailored to person's genomic make up – *precision medicine by white house*

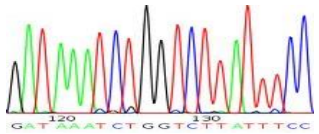
Big players latest trends

- Illumina's MiSeqDx and ThermoFisher's Ion PGM Dx cleared FDA approval for diagnostics usage and both companies will continue to seek product approvals– Illumina, Thermo Fisher Scientific
- Illumina founded a new company to enable cancer screening from a simple blood test. GRAIL will develop a pan-cancer screening test by directly measuring circulating nucleic acids in blood - Illumina
- Thermo Fisher Scientific acquired Affymetrix, a leading provider of cellular and genetic analysis products, to create new market opportunities in genetic analysis - Thermo Fisher Scientific

Source: Web search, media report

Various type of technologies have been developed and have been replaced

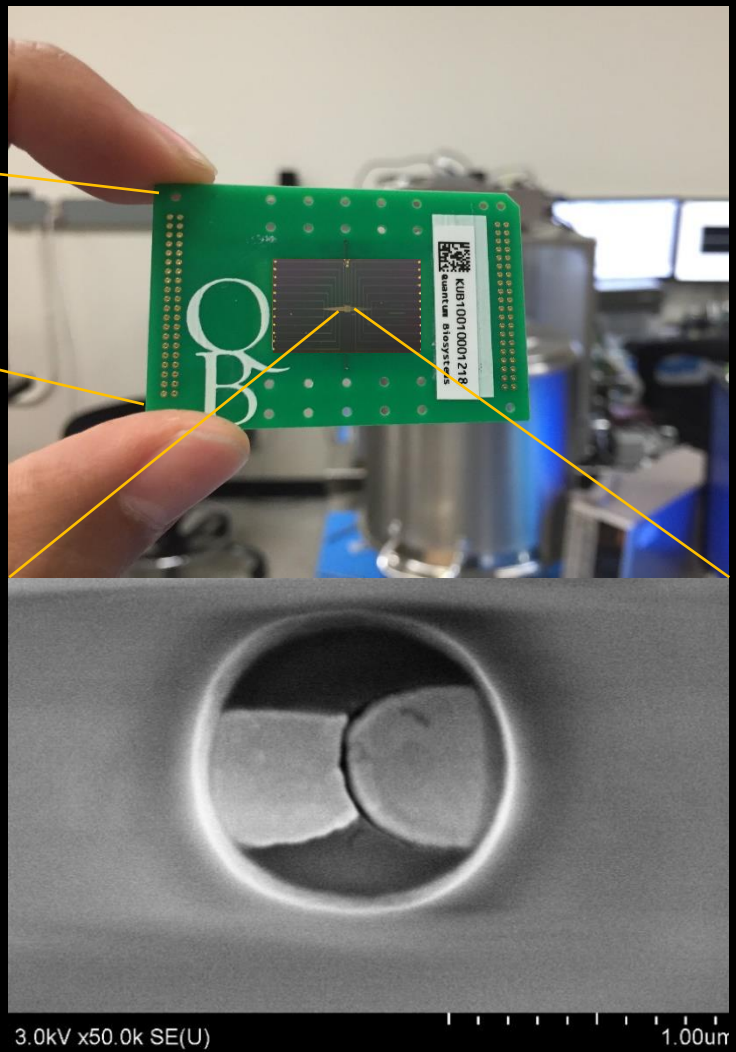
	1st Generation (~2005)	2nd Generation (2005~2011)	2.5 - 3rd Generation (2011~)	4th?
Technologies:	• Sanger method	• Sequencing by synthesis/ligasion • Parallel sequencing	• Non-optical detection (e.g. Electric signals, pH detection) • Simple sample preparation process • Single molecule detection	
Examples:	• ABI 3130 • ABI 3500 • ABI 3730(XL)	• Roche 454 • Illumina GA • Illumina HiSeq 2000 • Life Technologies SOLiD	• Pac Bio RS • Ion torrent PGM • Oxford Nanopore Technologies?	



Quantum Sequenceing™ : Single Molecule Synchronous Electrical Detection - First Breadboard Hardware and Semiconductor Chip

Hardware

Chip (Nano gap electrodes)



Source: QB

Summary of Quantum Sequencing strengths

- **Accurate** DNA and RNA sequencing - both normal and **epigenetically modified bases**
- **Low cost** instrumentation (no expensive optics) for use with much lower consumable cost than Ion Torrent
- **Highly scalable** systems - Density may be 10X-100X higher than Ion Torrent
- **Simple library prep** - No clonal amplification avoiding amplification bias and reducing library prep costs
- **Potentially longer read length** (compared to Illumnia, Ion Torrent) due to avoidance of dephasing issues

Source: QB

Core Management team

Toshihiko Honkura, MBA
President and CEO (Co-founder)

Toshi has a Master's degree in Analytical Biochemistry from the University of Tokyo (genome research project) and an MBA from Columbia University. Ten years' hands-on experience in business management and investment analysis as a manager at McKinsey & Company and the Innovation Network Corporation of Japan (INCJ), a public-private Japanese fund. Toshi's extensive scientific and business management skills and knowledge provide QB with excellent and tested leadership.

Takuma Nakatsuka, MBA
CFO (JP) and Director of Business Administration

Takuma has extensive management experience in pharma/ biotechnology industries, including as CFO of NanoCarrier, AnGes-MG and Nihon-Schering, as well as CEO of GenoMedia. Over 15 years of management experience in manufacturing and service industries. His career started in public service after graduation from the University of Tokyo (law). Graduate studies in public policy and economics at the University of Michigan and MBA from Wharton School, the University of Pennsylvania.

Christopher Pascoe, **CPA**
CFO / COO (US)

Over thirty years of international experience in the biotechnology and software industries. Founding CFO for several companies in these areas, and COO at two biotechnology companies, including Perlegen Sciences, a California genetic analysis and diagnostic testing company. Chris is a US CPA (PricewaterhouseCoopers) and a UK Chartered Accountant (Deloitte), with extensive international experience in establishing and managing strong financial and operational practices.

Source: QB

External Board Directors

Takehiko Sawabe, MS/MBA
Takehiko is a vice president of Healthcare Team of Innovation Network Corporation of Japan (INCJ). He has extensive experience in pharmaceutical and biotechnology industries. He concurrently serves on the boards of several life science startups including Anaeropharma Science Inc., Stella Pharma Corporation., Scohia Pharma Inc., and, Megakaryon Corporation. He received a master's degree in Pharmaceutical Science from the University of Tokyo and an MBA from Graduate School of Management, GLOBIS University.

Katsuya Hashizume
Katsuya is a Senior Associate of the Academic-Corporate Liaison Investment Group at JAFCO Co., Ltd., the largest venture capital firm in Japan. He focuses on seed/early stage high-tech startups. Katsuya earned a master's degree in Media and Governance from Keio University.

Naonori Kurokawa, PhD/MBA
Naonori is a partner at The University of Tokyo Edge Capital (UTEC) focusing on seed and early stage physical/life science investments. He serves on the boards of several high-tech startups, supporting academics and entrepreneurs who have industry-changing ideas. Naonori earned his PhD in Applied Physics from Osaka University and an MBA from the University of Chicago Booth School of Business.

Source: QB

R&D and IP leaders

Eric Nordman
Director of Hardware team
Twenty-eight years developing genetic analysis systems at Applied Biosystems. Lead systems engineer for several generations of DNA sequencing instrumentation, holding a number of patents in microfluidics, optics and capillary electrophoresis. In 2008 Eric was awarded the Distinguished Inventor Award from Applied Biosystems. Eric received his BS and MS from University of California, Berkeley.

Mark Oldham
IP/Technology Director
Mark has more than 25 years experience in biotech instrument R&D with Applied Biosystems and several other Next Gen sequencing companies. His experience has included biochemistry, electronics, mechanics, optics, firmware and software, together with single molecule sequencing, nanopore and nano-channel detection. Mark also spent 10 years working in the semiconductor fabrication field.

Hisao Kawasaki, PhD
Director of Semiconductor Chip team
Formerly a Manager for Texas Instruments in Japan and member of the US technical staff, Hisao then spent the last two decades working for Motorola in Austin, Texas as a Fellow of the Technical Staff and Manager of the Intrinsic Reliability Department,, where he was engaged in multi-level metallization and silicide process development. Doctorate in Electronic Engineering from Tohoku University.

Source: QB

Scientific Advisory Board

Tomoji Kawai, PhD
Tomoji is a specially appointed professor at the Institute of Scientific and Industrial Research, Osaka University, His specialty is single-molecule analysis technology. He is the lead researcher on the Kawai Project in which the Japanese government has invested thirty million dollars since 2009. The single-molecule analysis technology of this project is the core technology of Quantum Biosystems. Tomoji received his doctorate in from the University of Tokyo.

Latha Venkataraman, PhD
Latha received her BS in Physics from MIT followed by a PhD from Harvard University. She is an assistant professor in the Department of Applied Physics and Applied Mathematics at Columbia University. Prominent awards she has received include the National Science Foundation Career Award, Packard Fellowship for Science and Engineering, and the Alfred P. Sloan Fellowship in Chemistry.

Massimiliano Di Ventra, PhD
Massimiliano is a professor at the University of California, San Diego and a world-renowned theorist in condensed matter physics. He was the first to propose and support the sequencing by tunneling concept, a core idea behind both the FIRST Project and Quantum Biosystems. He was awarded his doctorate by the Swiss Federal Institute of Technology in Lausanne (Ecole polytechnique federale de Lausanne).

Yoshinobu Baba, PhD
Yoshinobu is a professor at the Graduate School of Engineering at Nagoya University. He is an expert on nanobiodevices and involved in multiple national-level projects in Japan. Chairman of Nagoya University's FIRST Research Center for Innovative Nanobiodevices. Co-creator of the FIRST-sponsored Kawai Project, and executive committee chairman of Nanobio Expo. Yoshinobu received his doctorate in Chemistry from the Kyushu University.

Source: QB

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How we set up Quantum Biosystems – the first three months

First meeting	Nov. (First week)	Osaka Univ visit
	Nov. (Second week)	Brainstorming meeting in Tokyo Univ
	Nov. (Third week)	Preliminary business plan
	Nov. (Forth week)	Discussion on setting up a start-up
Prep for corporation	Dec. (First week)	Discussion with family
	Dec. (First week)	Discussion with employer
	Dec. (First week)	Start prep for setting up a start-up
	Dec. (Second week)	Discussion with OU tech transfer office
	Dec. (Second week)	Prep for corporate registration
	Dec. (Second week)	Start searching corporate lawyer/IP lawyer
	Dec. (Third week)	Searching office space
	Dec. (Fourth week)	Contact VCs and potential strategic partners
Prep for Fund raising	Jan. (First week)	Corporate registration
	Jan. (First week)	Negotiation on Licensing with OU
	Jan. (First week)	Negotiation on strategic partnering
	Jan. (Second week)	Application of bridge financing (Japan Finance Corporation)
	Jan. (Fourth week)	Recruiting core internal/external members
Fund raising	March. (First week)	Bridge finance
	March. (Third week)	Exclusive licensing from OU
	March. (Third week)	Application for grant
	Apr. (Fourth week)	Equity finance ($1M)
	Apr. (Fourth week)	Grant acquisition ($2-3M)

Source: QB

Mindset for making the first step as an entrepreneur

- **Having courage to make the first bold move**
  - Do not need to have confidence for success, but need to have confidence for growth

- **Attracting talents and professionals**
  - Impactful goal setting
  - Realistic planning (step by step)
  - Reward beyond financial return

- **Working as an entrepreneur**
  - Continuous drive in uncertainties
  - Commitment to increase probability of success
  - Mindset change from “Flow” to “Asset”

Source: QB

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QB as one team across Japan and USA

Japan

Headcount (as of Jan 2017)

- Full time members: 9
  - Chip team: 3
  - Hardware team: 2
  - IP/PM: 1
  - Management/Admin: 3
- Part time members: 6 (including advisory members)

R&D roles

- Chip design, manufacturing and testing
- Electrical circuits and components development

U.S.

- Full time members: 13
  - Hardware team: 6
  - Informatics: 4 (incl. UK)
  - Management/Admin: 3
- Part time members: 5 (includes 4 Hardware consultants)

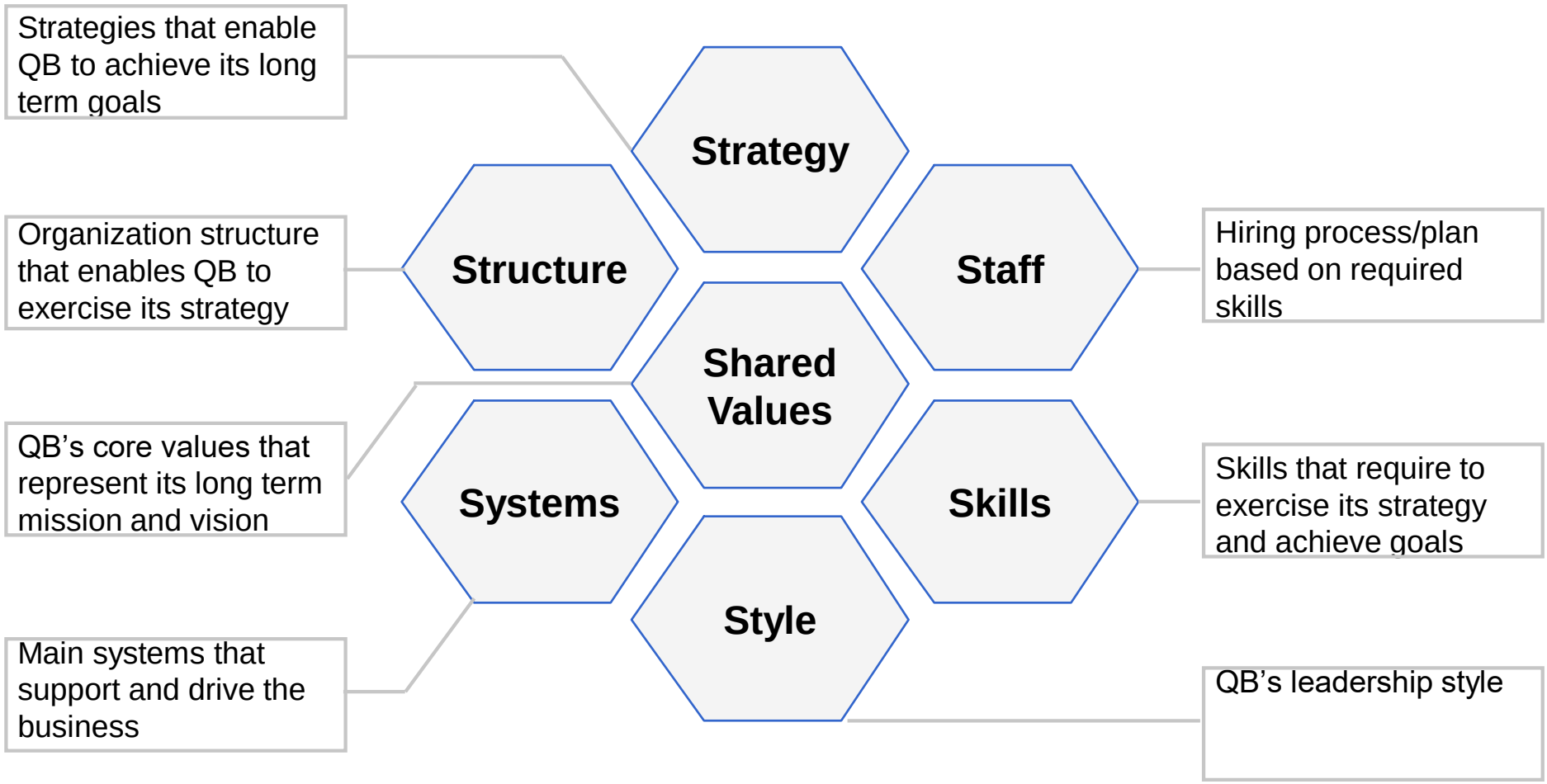
- Hardware/Fluidics design, system development
- Data measurement and system optimization
- Algorithms development and data management

Source: QB

Can east samurai spirit meet western (Sillicon Valley) entrepreneurial spirit?

source: Red Sun (1971)

Guiding principle for aligned decisions making in QB



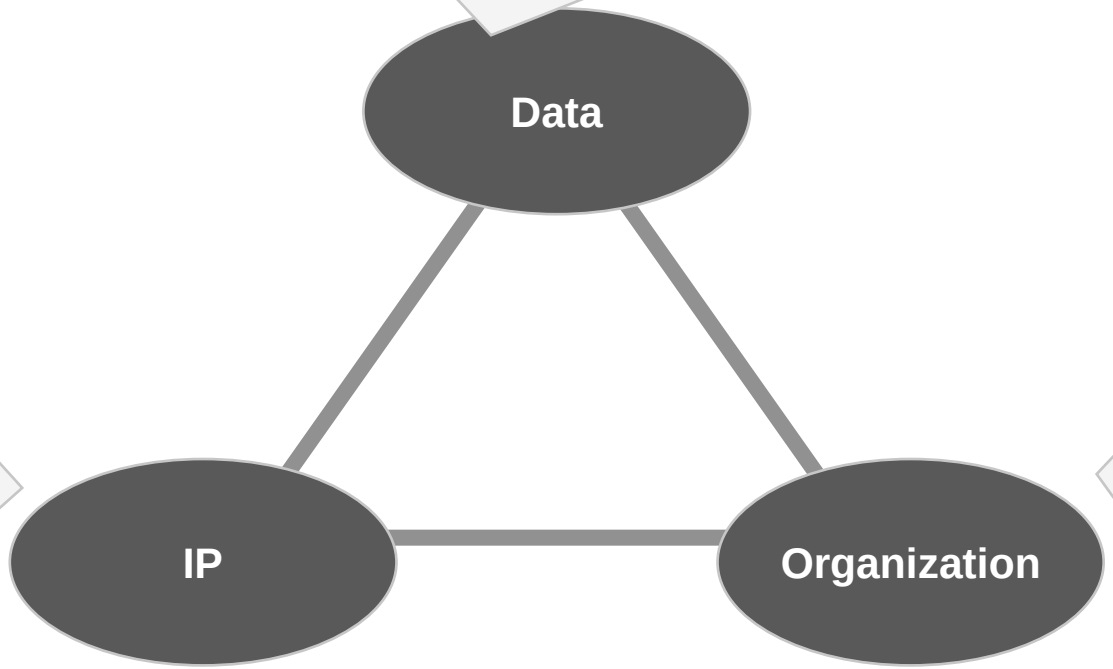
Shared Values – QB's visions

Becoming the leading global organization to develop world first solid-state quantum sequencing platform*, which can unlock the value of massive amount of genomic/epigenomic data

Source: QB

Strategy – Data, IP, and Organization are three fundamental sources of value

- QB's core source of value - No companies have quantum sequencing data, platform nor metrics for the data



- Barrier to entry for generating data
- Data support strong/unique IP filings

- Data and IP attracts talent
- Talents attract talents
- Talents generate data and IP

Source: QB

Organizational change towards global start-up

- **Cultural and organizational transformation with the right “start-up” mindset**
  - Transformation in R&D - from “Japanese University” to “Global Start-up”
  - Implement the right “Start-up mindset” (incl. “Fail fast, Fail forward” - accelerating PDCA cycles with rapid decision makings)

- **Better and frequent communication as a global start-up**
  - English is the official language of R&D and business (and for global start-up).
  - Better and frequent communication will become an important part of evaluation

- **Expanding presence and network in the community**
  - Comprehensive support for global business and R&D together with strong Admin capabilities (incl accounting, business trip, IT system etc)
  - Right (internal/external) incentive and system to increase presence in the global community

Key Success Factor for University backed startups is separating its early stage basic research and product development

	University researches	Technology start-ups
Objective of R&D	**Basic Research** – Publishing articles by innovative research with champion data	**Product Development** - Commercializing reliable product with reproducible data
Metaphor	Making an F-1 car for a season	Manufacturing commercial passenger cars
Objective of R&D	Inventing cutting-edge technology to improve top-notch performance	Producing safe, durable, comfortable and less costly cars
Users (Drivers)	Only professional drivers can drive the F-1 car	Ordinary persons should be able to drive the car

Challenge

- At university backed startups, it is a typical challenge to focus its R&D objective and separate basic research from product development since university research's objective (Early stage research) and startup's objective (product development) is different

Source: QB

Style – All level of professionals exert leadership with understanding of the QB's style leadership

QB's leadership style

Managing Diversity

- Respect diversity with frequent and clear communication with people with multi-cultural/、technological background.

Collaborative problem solving

- Actively seek collaboration opportunities with internal and external specialists to accelerate goal achievement

Maintaining Transparency

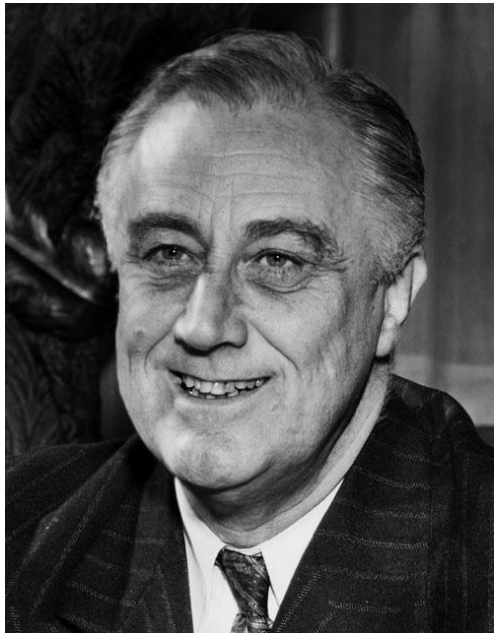
- Being transparent about the progress/status, role/responsibility and achievement which can be accessible by all the members

Professionalism (Goal focused, Commitment to result, Complete work)
+
Entrepreneurial mindset (Risk taking, Action oriented, Proactiveness)

Source: QB

Franklin Delano Roosevelt

“It is not the critic who counts; not the man who points out how the strong man stumbles, or where the doer of deeds could have done them better. The credit belongs to the man who is actually in the arena, whose face is marred by dust and sweat and blood, who strives valiantly; who errs and comes short again and again; because there is not effort without error and shortcomings; but who does actually strive to do the deed; who knows the great enthusiasm, the great devotion, who spends himself in a worthy cause, who at the best knows in the end the triumph of high achievement and who at the worst, if he fails, at least he fails while daring greatly. So that his place shall never be with those cold and timid souls who know neither victory nor defeat.”



ただ批判するだけの人に価値はない - 強い人のつまずきを指摘し、やり手ならもっとうまくできたはずだとあげつらう人だけの人には。

称賛に値するのは、実際に競技場に立ち、埃と汗と血にまみれながらも勇敢に戦う人だ。あるときは間違いをおかし、あと一歩で届かないことが何度もあるかもしれない。何をするにも間違いや欠点はつきまとう。それでもなお、ことを成し遂げるためにもがき苦しみ、情熱に燃え、力を尽くし、体技のために身を粉にして励む人こそ偉大なのだ。

順風ならば最後には勝利に輝くだろうし、最悪の場合、失敗に終わるかもしれない。だが彼らは、少なくとも果敢なる挑戦をしたのである。その人物は、勝利も敗北も知らない臆病者たちとは一線を画している。

Source: Web Search (Flanklin Roosevelt)