

CLOUD BIOLOGY

A short introduction



Valentin Zulkower
Edinburgh Genome Foundry
BBSRC Skills School, June 4th, 2018



Program

Labs are increasingly outsourcing their bench work.
We will give an overview of that trend:

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- ▶ **What happens after you click "order"** in the particular example of the EGF.

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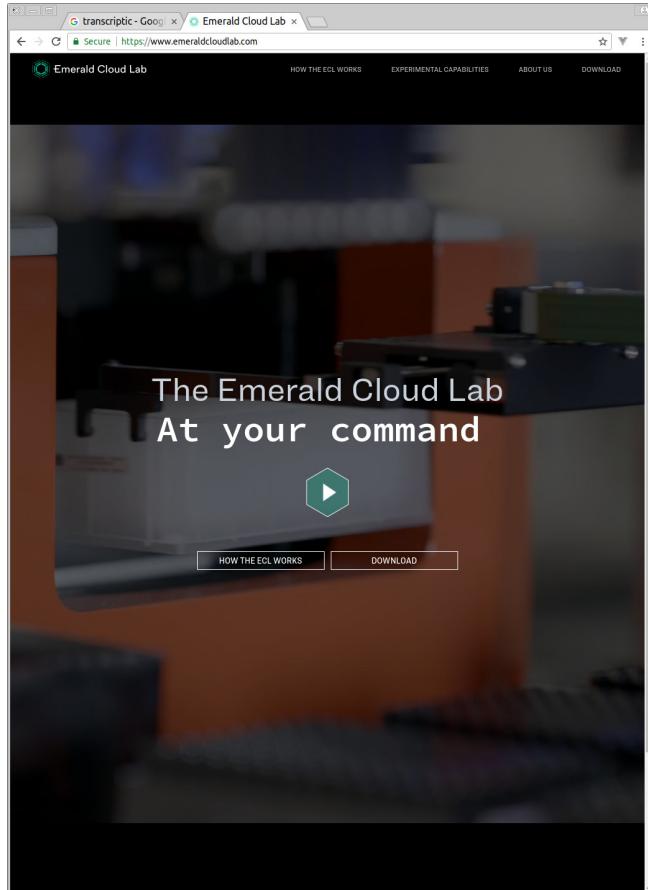
- ▶ **A few examples of cloud biology** in industry and academia.
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Tomorrow we will look closer at how software can help you assemble DNA without thinking too much.

A few examples of cloud biology



Some automated facilities in the world



Emerald Labs

Founded 2010

*Sweep aside the daily
laboratory grind, and allow
day-to-day work to center
on orchestrating science*

- ***emeraldcloudlab.com***

Some automated facilities in the world



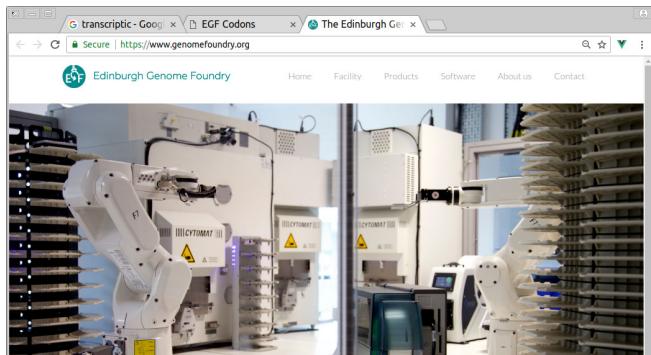
Transcriptic

Founded 2012

Make it possible for two postdocs with a laptop in a coffee shop to run a drug company.

- Max Hodak, Founder & CTO

Some automated facilities in the world



Edinburgh Genome Foundry

Robotic Precision. Academic Expertise.

The Edinburgh Genome Foundry (EGF) is a research facility specialised in the assembly of large DNA fragments using a highly automated platform.

[MORE ABOUT US](#)

DNA Design, Assembly, Testing

... and much more ! Discover our catalogue of products and services for industrial and academic research groups in the UK and beyond.

[OUR SERVICES](#)

Try our Software Suite

EGF

Founded 2014

Enable high-throughput projects and provide DNA assembly expertise in the UK and beyond.

(note: we need to say something cooler for next time)

Sequence design software

The screenshot shows the Autodesk Genetic Constructor software interface. On the left, there's a tree view of 'EMMA Templates' and a 'New Construct'. A central workspace shows two constructs:

5 - Episomal, single bicistronic unit

Position 3	Position 6	Position 7	Position 8a	I-I	Position 8b
TRE35p	Nt-MLS	L7Ae - Weiss	Ct - INDEL		
CMVp_Tet	ATG-BoxC (L7Ae)	mNeoGreen			
EF1ap	Nt-SV40-NLS	Bx8I			
CAGp	Kozak_ATG	Flycatcher Luciferase			
	Nt-myristoylation signal	mKate2			
	3X-FLAG	L7Ae			
	Nt-Palmitylation sequence	mTagBFP2			
	Nt-IgKL sequence	mRuby2			

Position 9 Position 11 Position 25

- NeoR
- SVA40 polyA
- Flycatcher Luciferase -3XFLAG
- mRuby2
- mNeogreen
- PuroR
- a-Tubulin
- BSGp
- DmC
- mTagBFP2

6A - Episomal, Two bicistronic units

Position 3	Position 6	Position 7	Position 8	I-I	Position 9
TRE35p	ATG-BoxC (L7Ae)	mRuby2	p3A-Porcine teschovirus-1	BSGp	
CMVp_Tet	Kozak_ATG	mKate2	Linker 1	mTagBFP2	
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	Nt-MLS	L7Ae		DmC	
	Nt-SV40-NLS	mNeoGreen		a-Tubulin	
	3X-FLAG	Flycatcher Luciferase		NeoR	
				Flycatcher Luciferase -3XFLAG	

A sidebar titled 'Tutorials' is open, showing a 'Beginner' section with a 'Getting started' link and a brief introduction to the software.

[Secure | https://benchling.com/tlouu/bd7c0q4n-drachise/seq-ju-mak-p2_bxb1_attp_tg/edit](https://benchling.com/tlouu/bd7c0q4n-drachise/seq-ju-mak-p2_bxb1_attp_tg/edit)

p2_Bxb1_attP_TG

Sequence_1

test

Bxb1 attP

tonB terminator

cat promoter

KanR

BASES 1867

ASSEMBLY WIZARD ▾ **SPLIT WORKSPACE**

Autodesk Genetic Constructor

Benchling

Protocol management software

The screenshot shows the homepage of protocols.io. At the top, there's a search bar with placeholder text "Search...". Below it, a large search input field has "Search researchers" and a prominent orange "SEARCH" button. A network graph visualization is overlaid on the background. Below the search area, a section titled "Try one of these popular searches:" lists various categories with corresponding icons: Buffers, Media, Western Blots, Computational workflows, RNA Extraction methods, Immunohistochemistry, Tutorials, and Clinical trials. Further down, there are links to "Browse:" and "Protocols Groups". The footer contains links for "ABOUT US", "PARTNER WITH US", "SUPPORT", and "LEGAL", along with social media icons for Twitter and Facebook. A small cookie consent banner at the bottom states: "The protocols.io website uses cookies. By continuing to browse the site, you accept our use of cookies, [Privacy Policy](#) and [Terms of Use](#)".

protocols.io

The screenshot shows the Riffyn SDE Overview page. The background is a blue-tinted photograph of laboratory glassware. At the top, there's a navigation bar with links for "SDE OVERVIEW", "IMPACT", "CASE STUDIES", "BLOG", "MORE", and "CONTACT". A call-to-action banner says "NEVER MISS A DISCOVERY". In the center, a quote reads: "The Riffyn SDE supports every step of discovery & development" followed by a testimonial: "'Riffyn makes data sharing, tracking, and data analysis seamless. It's no longer a moment of panic to track down someone for methods or data.'".

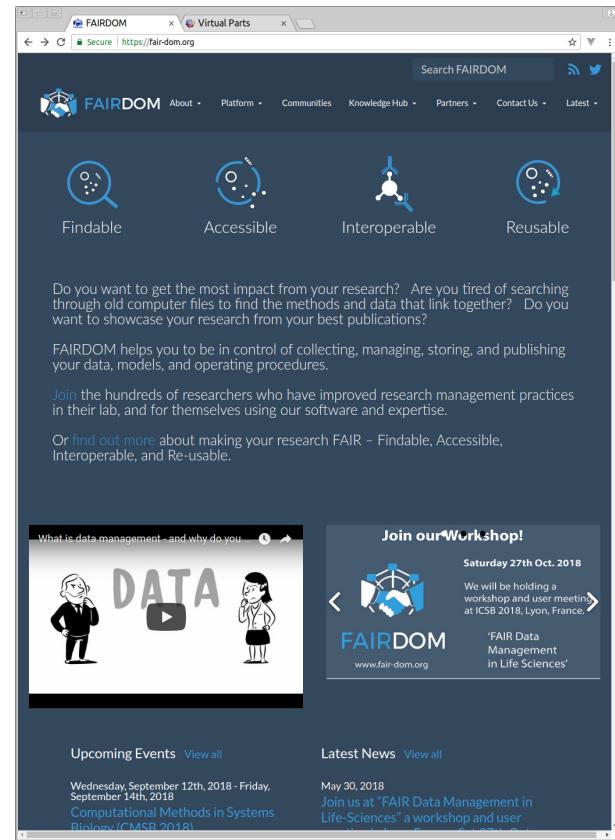
Riffyn

Data repositories



The screenshot shows the homepage of SynBioHub. At the top, there's a navigation bar with links for "Submit", "About", "Login or Register", and a "Home" link. Below the navigation is a large orange header with the "SynBioHub" logo and the text "SynBioHub is a design repository for people designing biological constructs. It enables DNA and protein designs to be uploaded, then provides a shareable link to allow others to view them. SynBioHub also facilitates searching for information about existing useful parts and designs by combining data from a variety of sources." There are three main call-to-action sections: "Search for useful parts and designs" (with a search bar), "Upload your design for safekeeping" (with an upload icon and "Submit a Design" button), and "Share designs for publication or collaboration" (with a share icon and "Manage Submissions" button). At the bottom, there's a copyright notice: "© 2018 Newcastle University, University of Utah, and collaborators" and links to "About SynBioHub", "View Source on Github", and "Report an Issue".

SynbioHub



The screenshot shows the homepage of FAIRDOM. The top navigation bar includes links for "About", "Platform", "Communities", "Knowledge Hub", "Partners", "Contact Us", and "Latest". Below the navigation, there are four icons representing FAIR principles: "Findable" (magnifying glass), "Accessible" (DNA helix), "Interoperable" (cloud with arrows), and "Reusable" (circular arrow). A central text block asks, "Do you want to get the most impact from your research? Are you tired of searching through old computer files to find the methods and data that link together? Do you want to showcase your research from your best publications?" It continues, "FAIRDOM helps you to be in control of collecting, managing, storing, and publishing your data, models, and operating procedures." It encourages users to "Join the hundreds of researchers who have improved research management practices in their lab, and for themselves using our software and expertise." It also mentions, "Or [find out more](#) about making your research FAIR – Findable, Accessible, Interoperable, and Re-usable." On the right side, there's a section for an upcoming event: "Join our Workshop! Saturday 27th Oct. 2018" at ICSB 2018 in Lyon, France. It includes a "FAIRDOM" logo and the URL "www.fair-dom.org". Below this, there are sections for "Upcoming Events" (listing a conference from September 12-14, 2018) and "Latest News" (mentioning a workshop at CMSB 2018).

Globalized pathway engineering (from true stories)



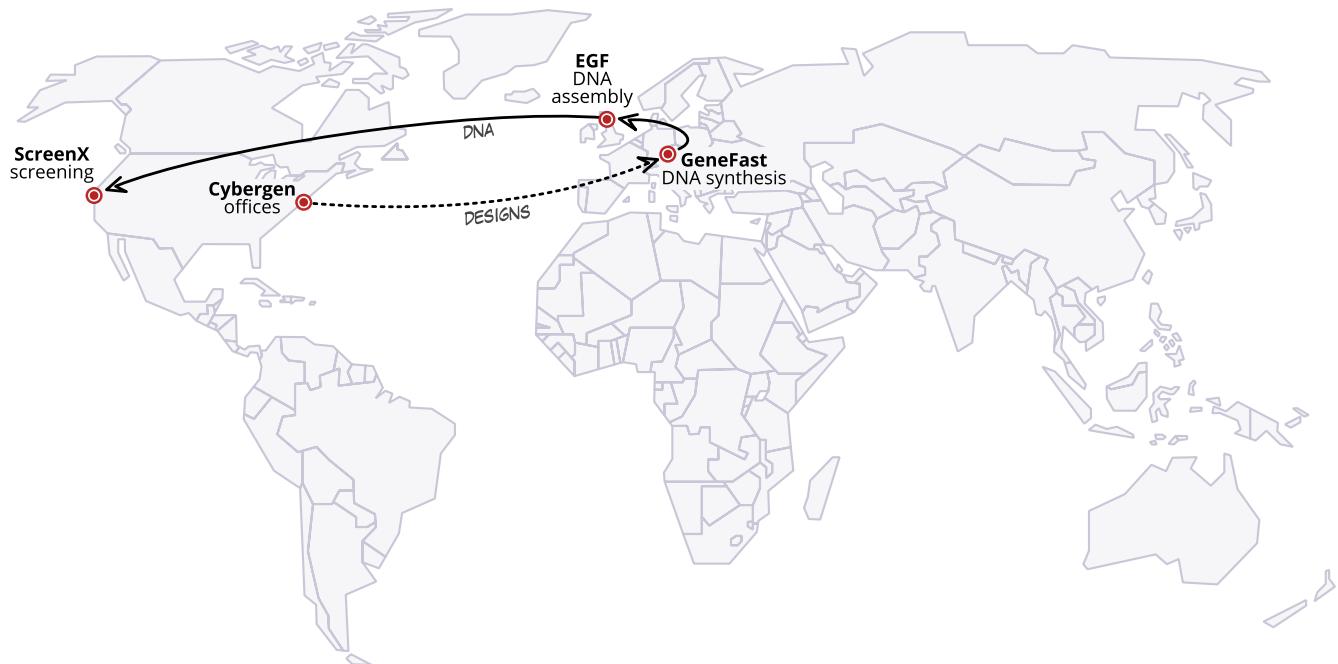
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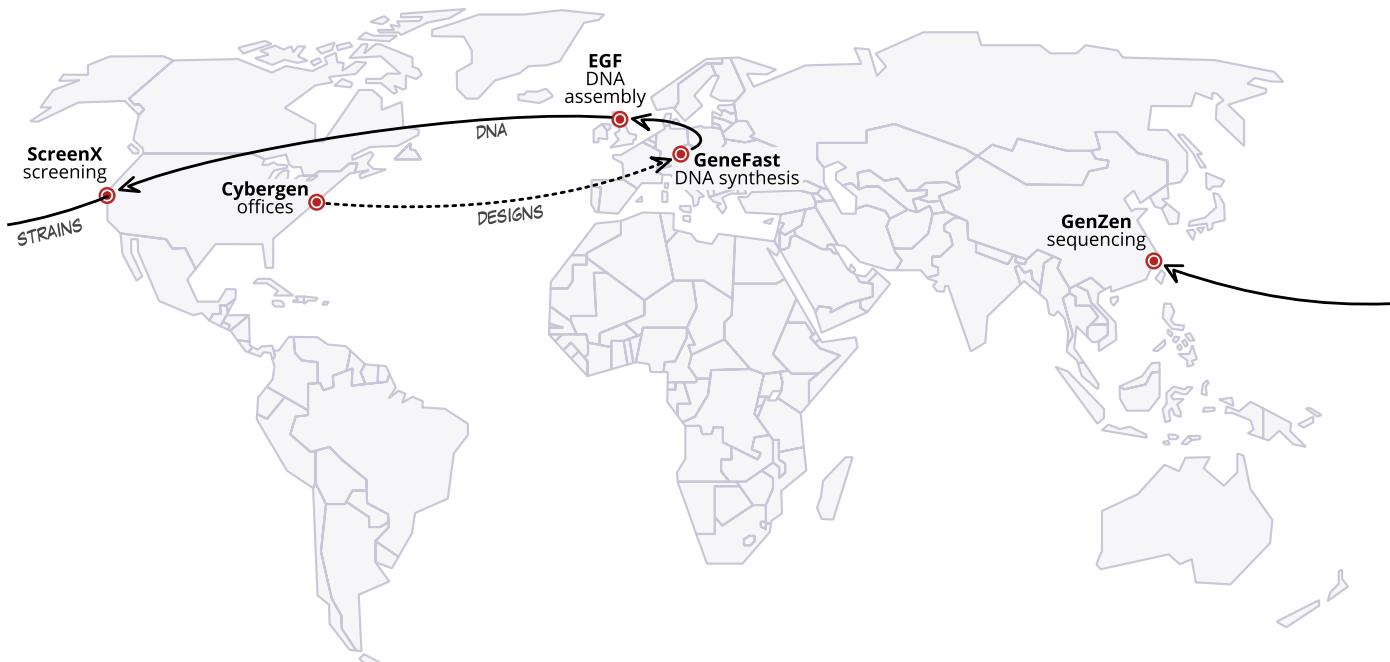
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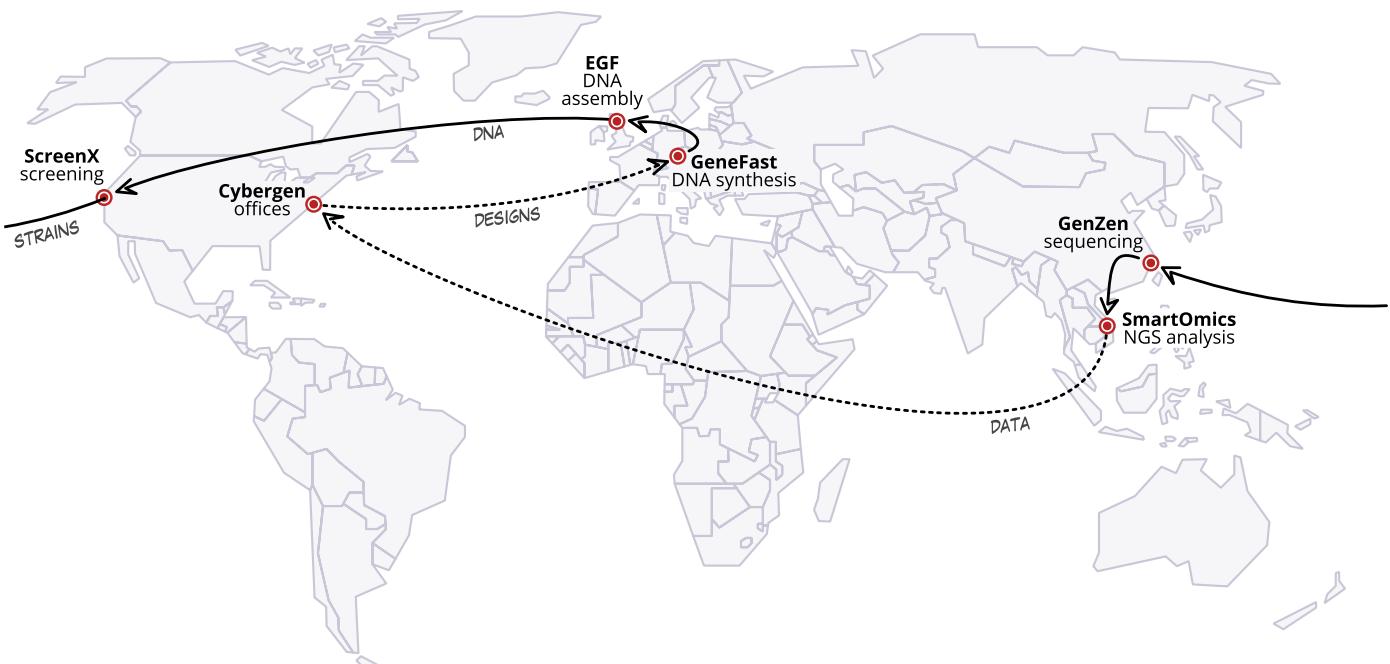
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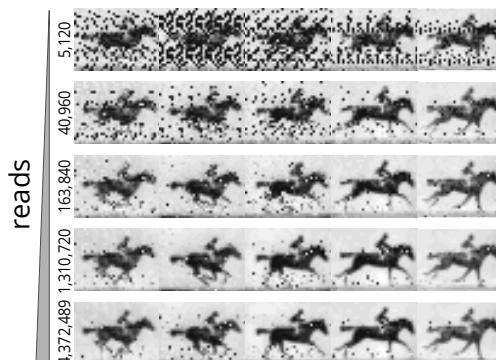


CRISPR–Cas encoding of a digital movie into the genomes of a population of living bacteria

Seth I . Shipman^{1,2,3}, Jeff Nivala^{1,3}, Jeffrey D. Macklis² & George M. Church^{1,3}

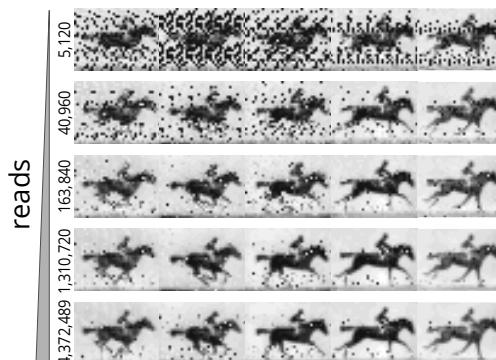
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METHODS

Data reporting. No statistical methods were used to predetermine sample size. The experiments were not randomized. Colony counts were performed blind to experimental condition using Amazon's Mechanical Turk, the investigators were

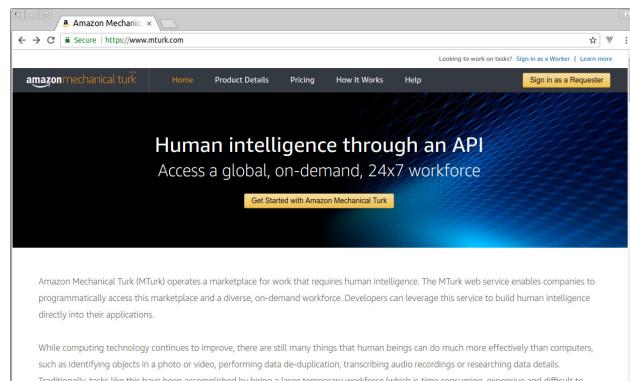
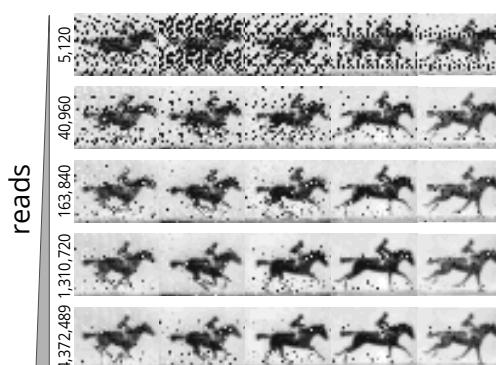
Cloud biology in academia

nature

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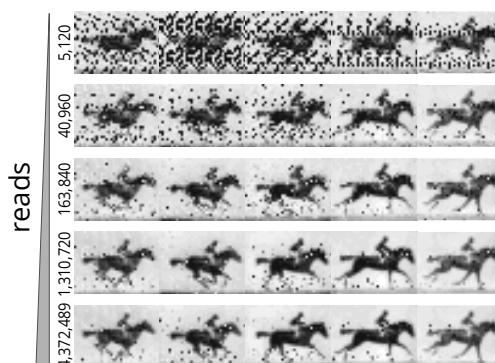
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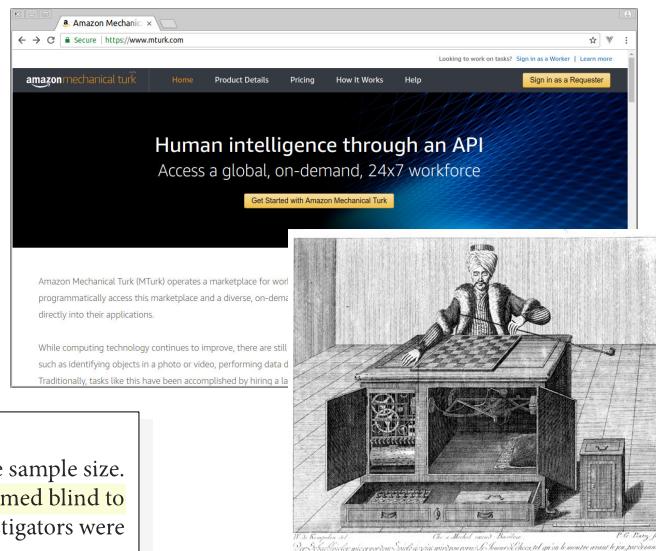
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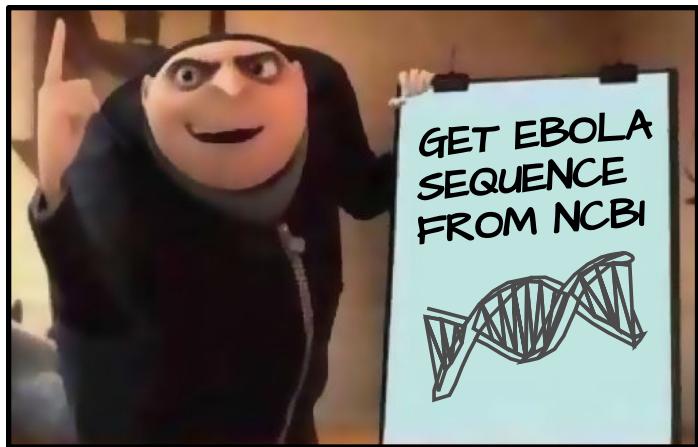
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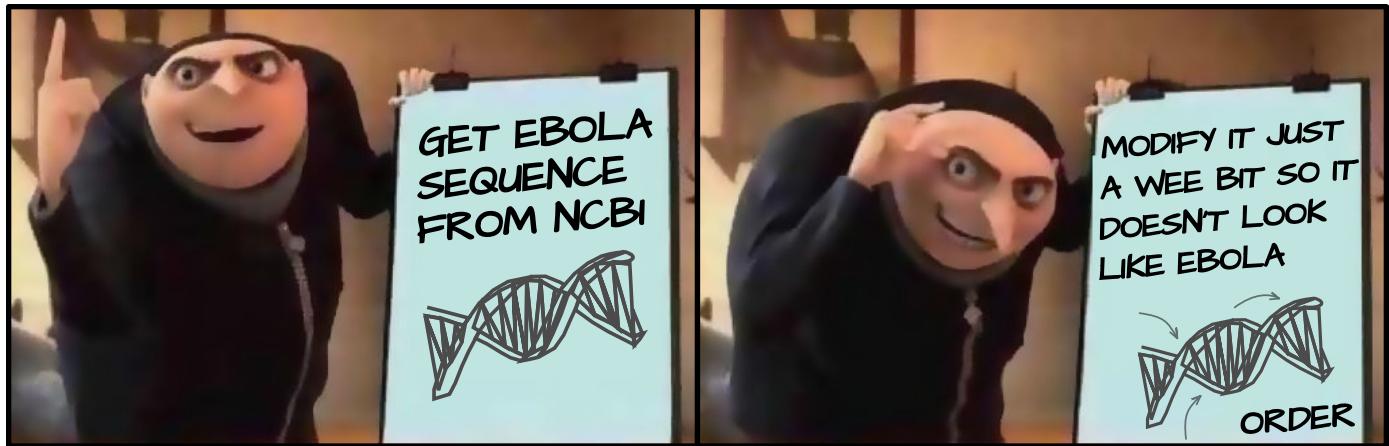


How do we keep cloud biology safe ?

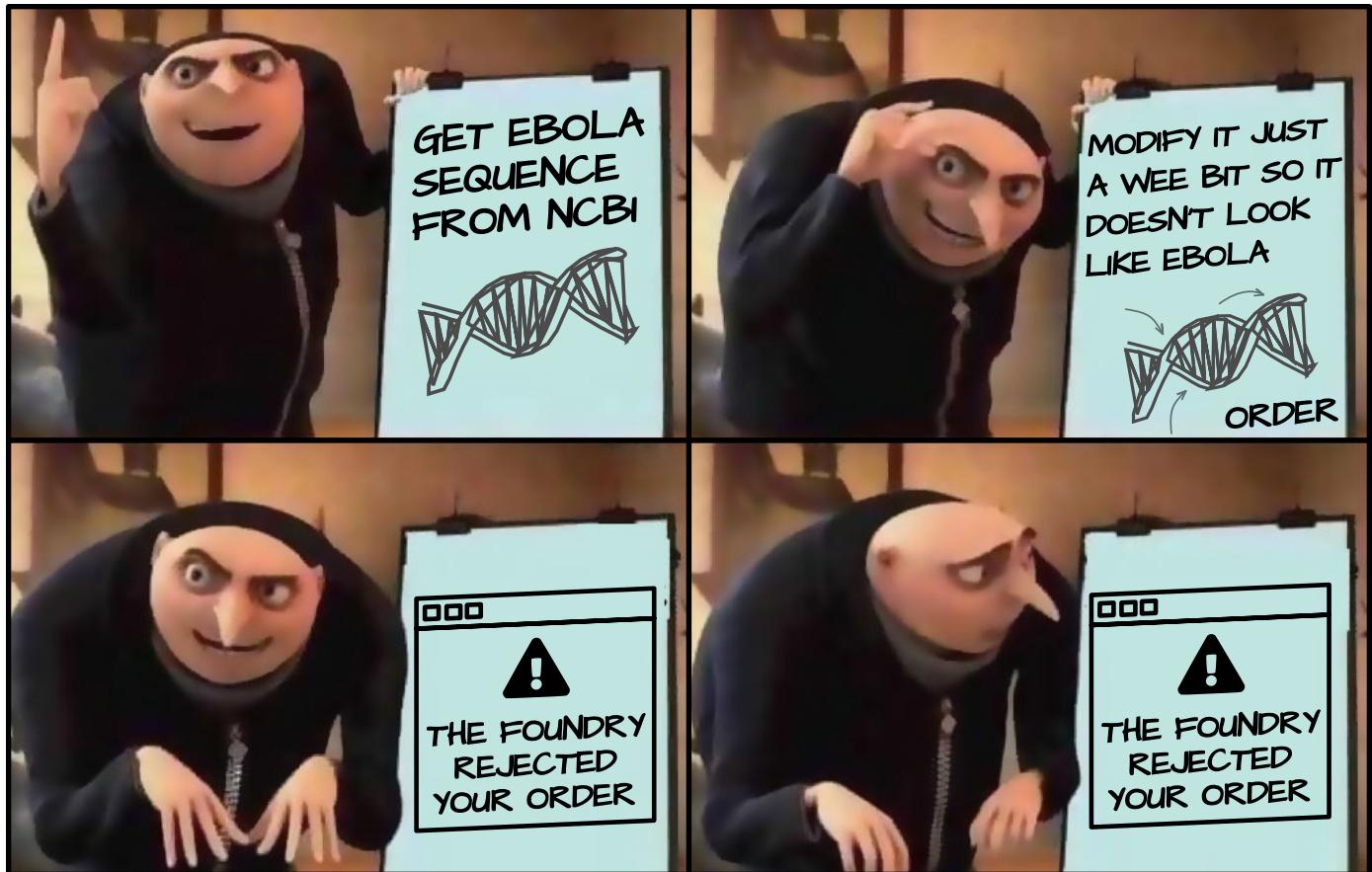
Challenge : Pathogenicity screening



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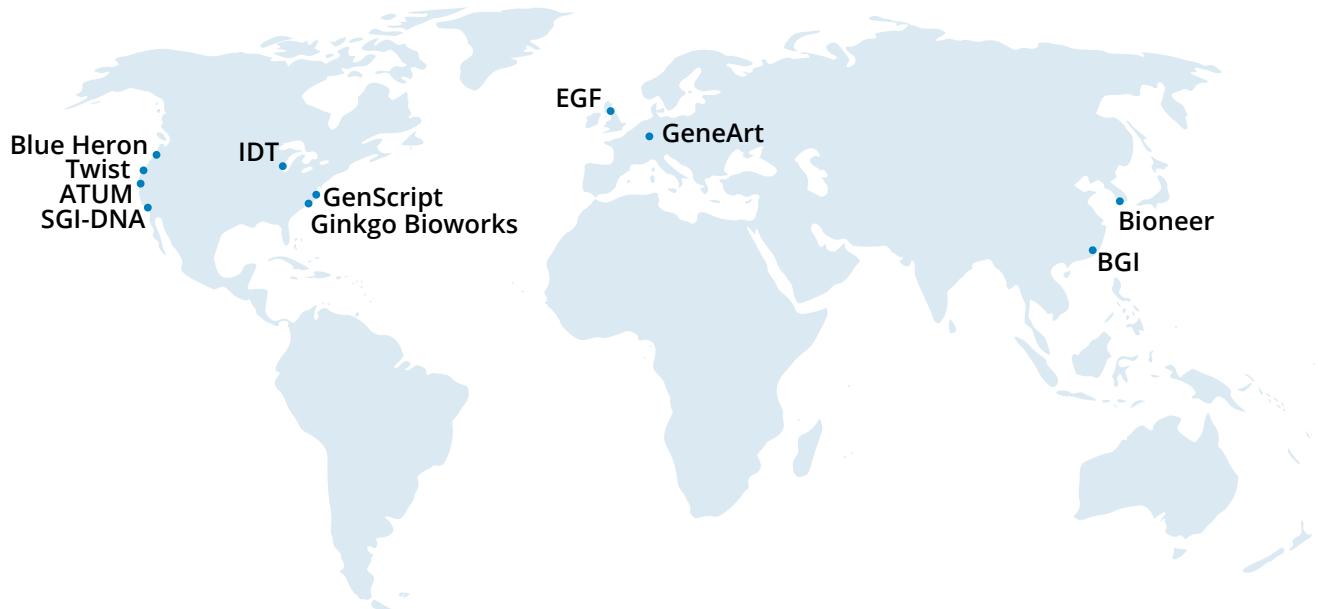
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The International Gene Synthesis Consortium



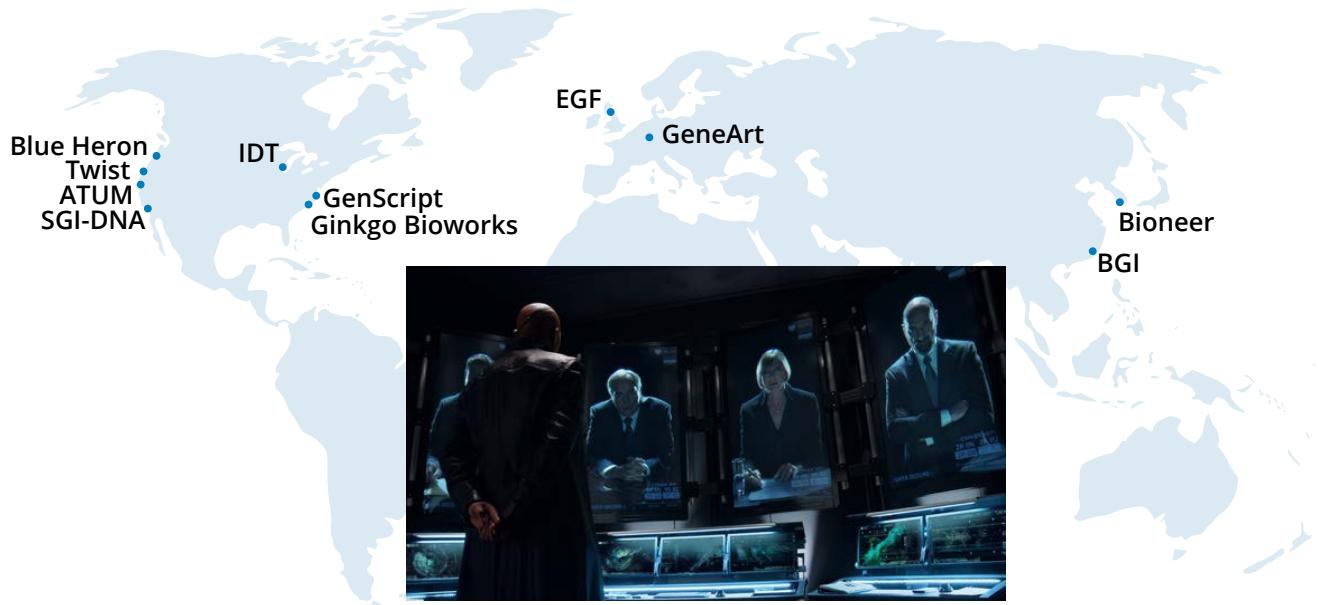
International
Gene Synthesis
Consortium



The International Gene Synthesis Consortium



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Monthly teleconference (kind of)

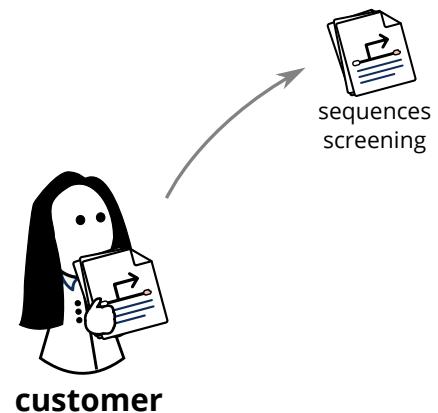
Pathogenicity screening with the IGSC protocol

Pathogenicity screening with the IGSC protocol

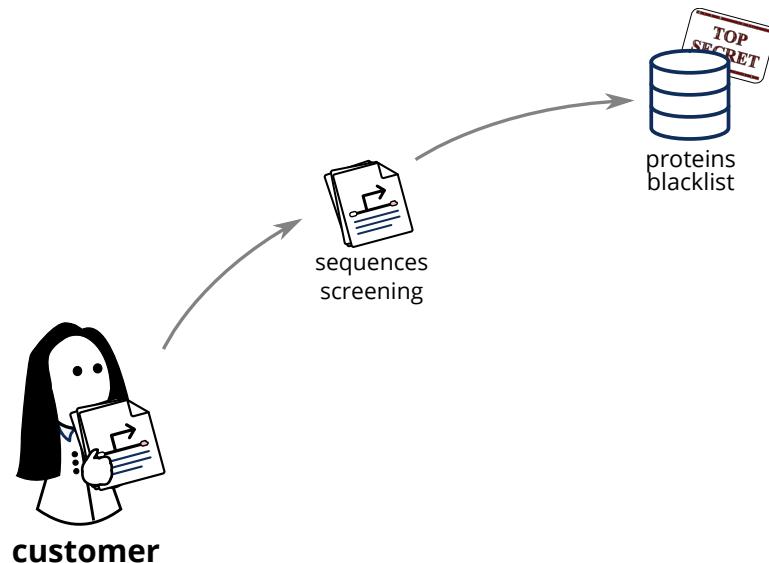


customer

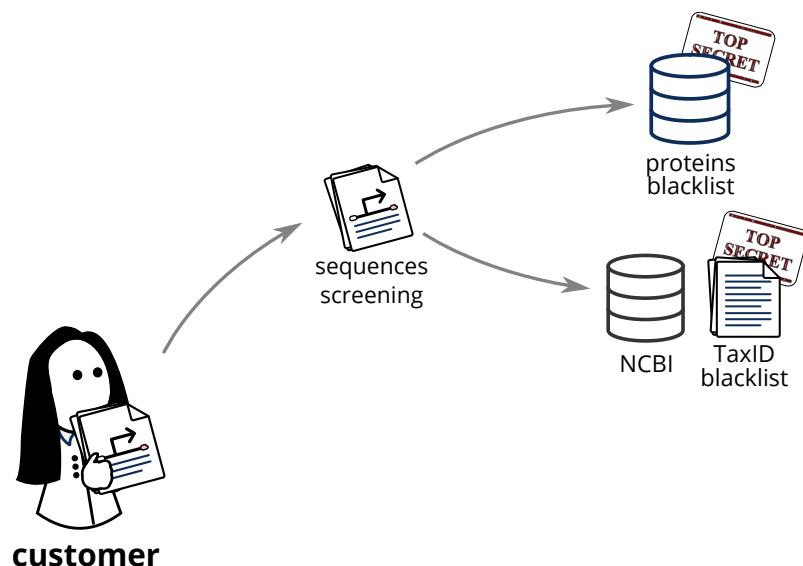
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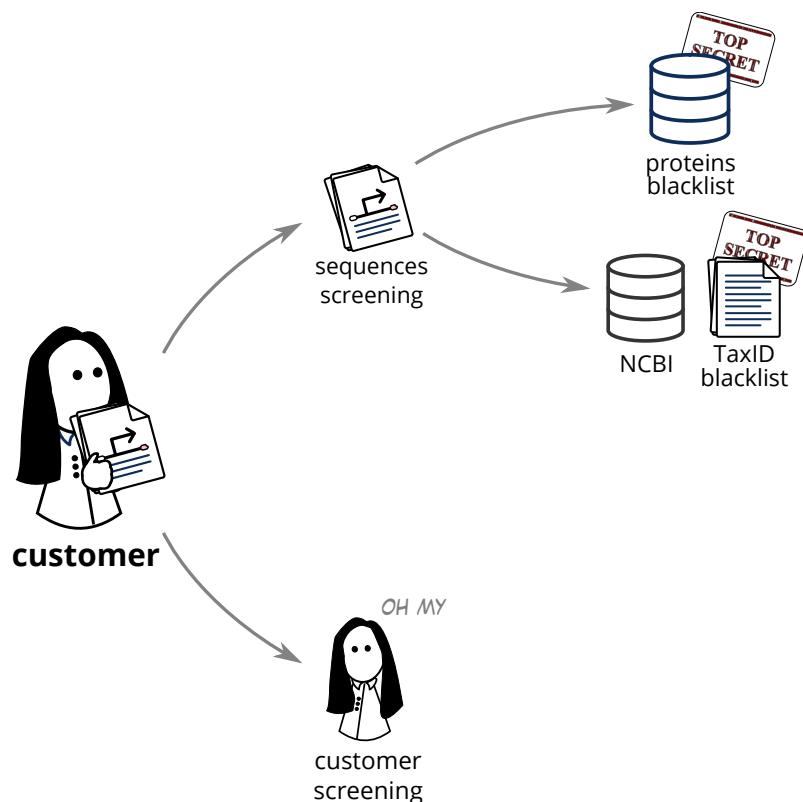
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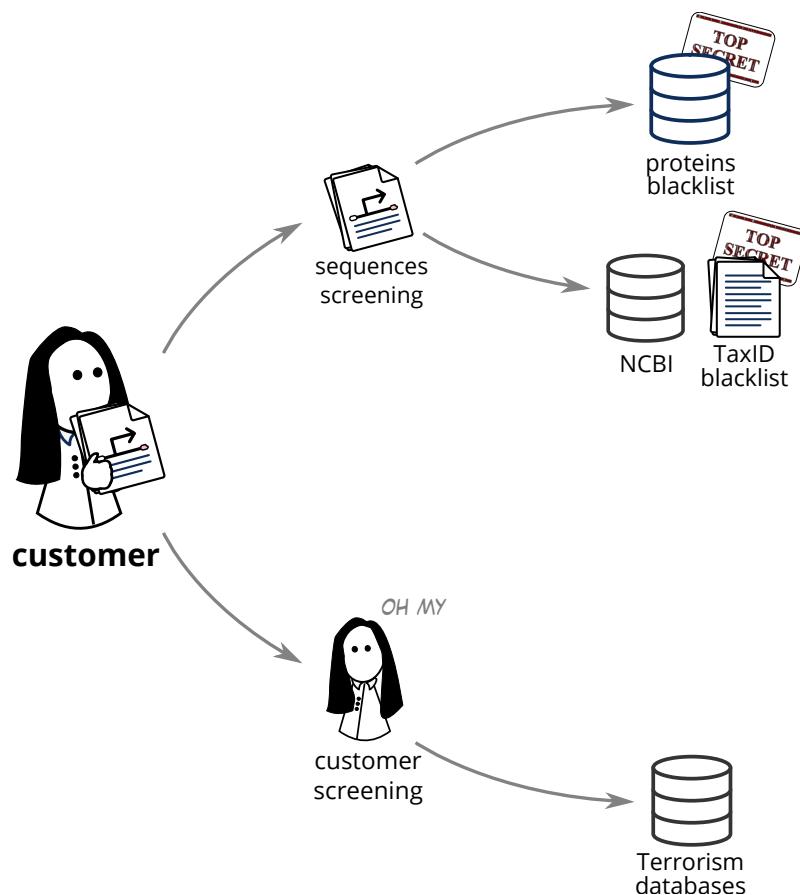
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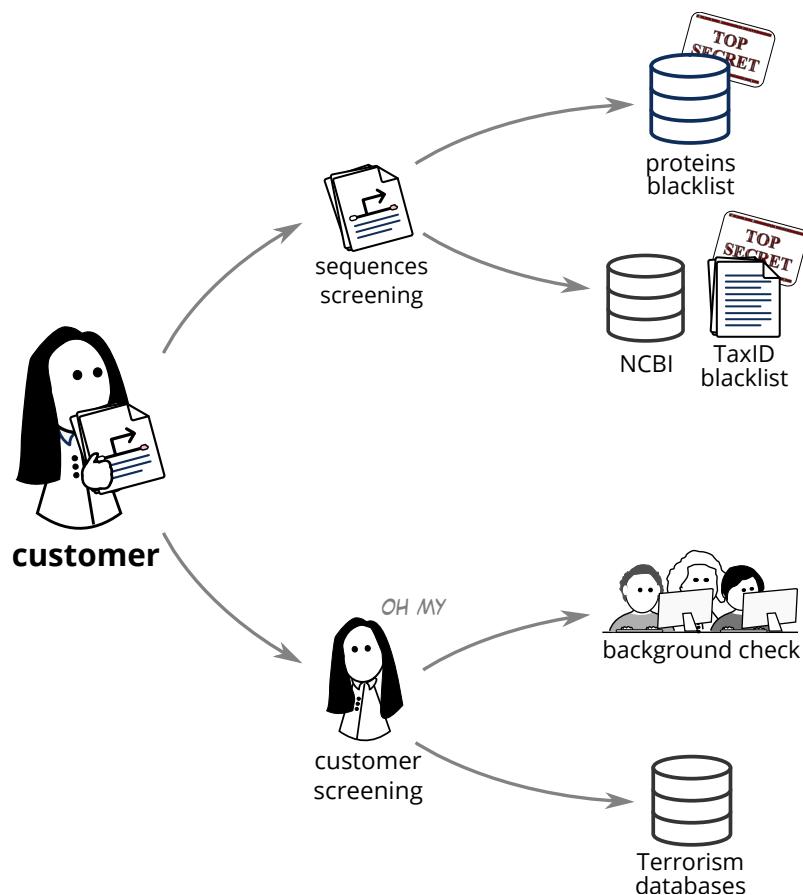
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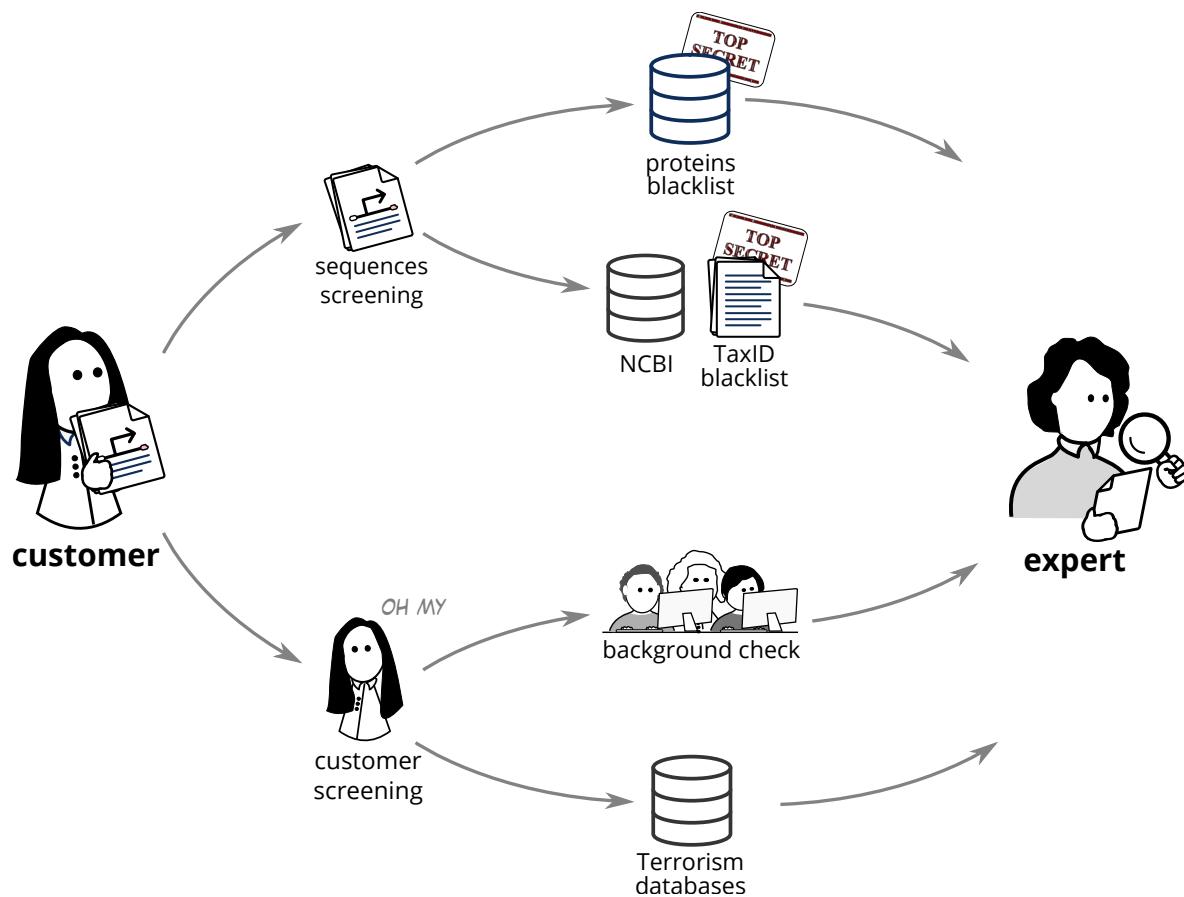
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- ▶ Sequences can be obfuscated (codon juggling, fragmentation...)
- ▶ Pathogen databases must keep up with discoveries
- ▶ Not all genes in a pathogen organism are pathogenic

Note: legitimate projects also raise eyebrows

The screenshot shows a web browser displaying a news article from the journal *Science*. The URL in the address bar is www.sciencemag.org/news/2017/07/how-canadian-researchers-reconstituted-extinct-poxvirus-10000.... The page features a dark header with the *Science* logo and navigation links for Home, News, Journals, Topics, and Careers. A search bar and a 'Become a member' button are also visible.

The main content includes a large image of several virus particles under a microscope, with a 'SHARE' button showing 121 shares across various platforms. Below the image, a caption reads: "An unpublished study suggests that making variola, the virus that causes smallpox, is neither expensive nor difficult." The source is cited as "EYE OF SCIENCE/SCIENCE SOURCE".

The headline of the article is "How Canadian researchers reconstituted an extinct poxvirus for \$100,000 using mail-order DNA". The byline is "By Kai Kupferschmidt | Jul. 6, 2017, 5:00 PM". A short summary at the bottom states: "Eradicating smallpox, one of the deadliest diseases in history, took humanity decades and cost billions of dollars. Bringing the scourge back would probably take a small scientific team with little".

Note: DNA sequences *could* also target software

The screenshot shows a web browser window displaying the MIT Technology Review website. The URL in the address bar is <https://www.technologyreview.com/s/608596/scientists-hack-a-computer-using-dna/>. The page features the MIT Technology Review logo and navigation links for Log in / Create an account, Search, Topics+, The Download, Magazine, Events, More+, and Subscribe. A banner at the top reads "Think Big. Take Risks. INNOVATE!" with a phone number 703.808.2769. Below the banner, the main headline is "Scientists Hack a Computer Using DNA". A subtext below the headline states: "Malware can be encoded into a gene and used to take over a computer program." To the right of the text is a photograph of a gloved hand holding a clear plastic test tube or vial.

Note: DNA today vs. 80's *supercomputers*

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... The United States should not sell India anything with a possible nuclear application, such as the supercomputer now being considered

from **India's Nuclear Cover-Up**
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BioXp benchtop cloner (SGI-DNA)

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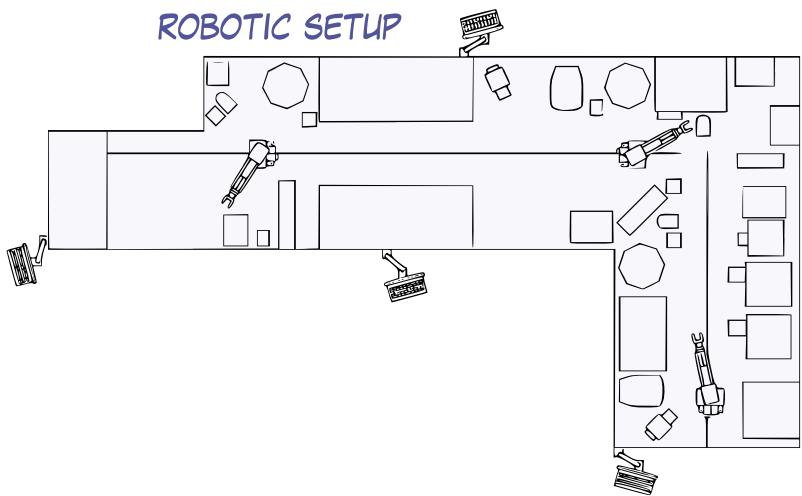




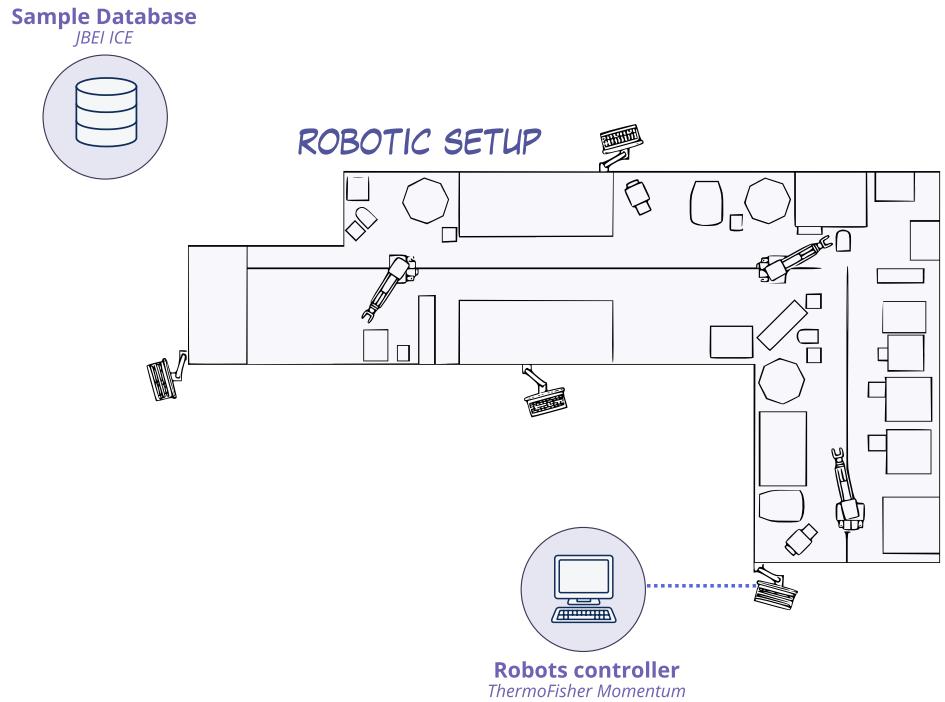
What happens after you click *Order* ?



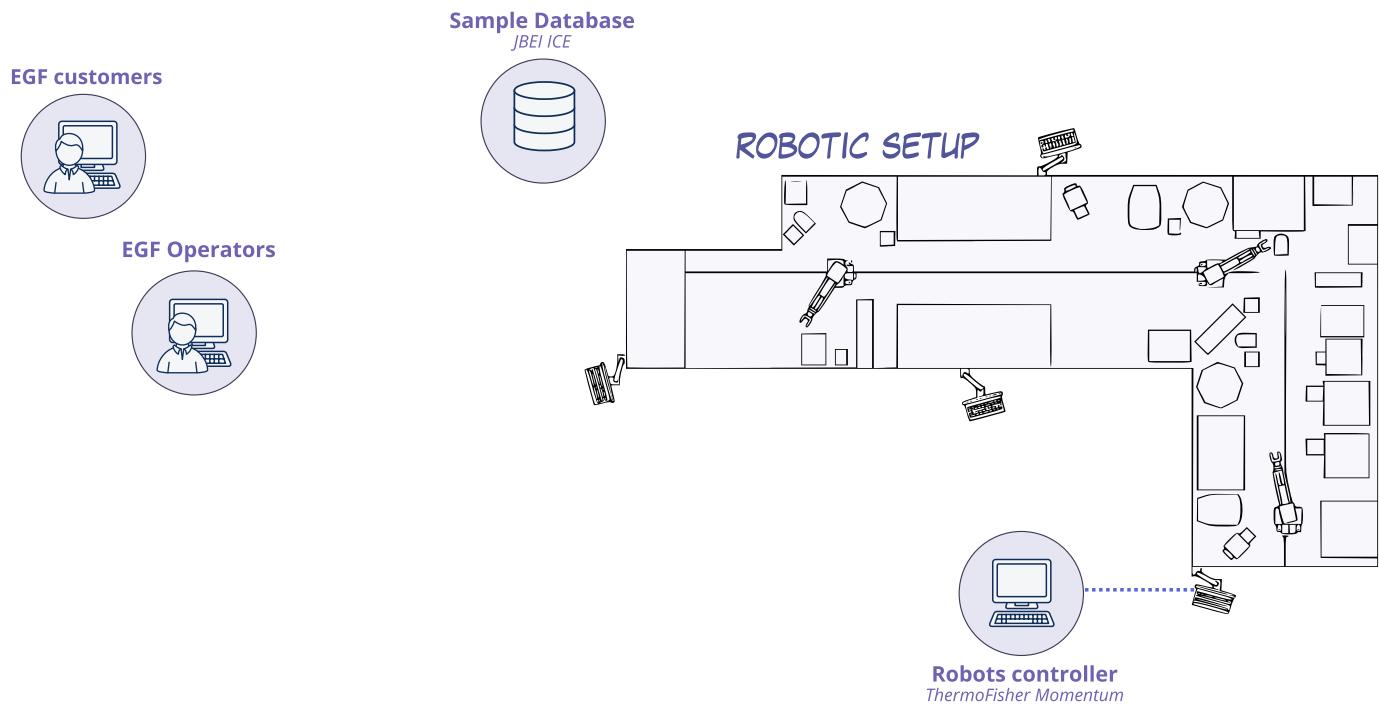
The EGF software, a layer between humans & machines



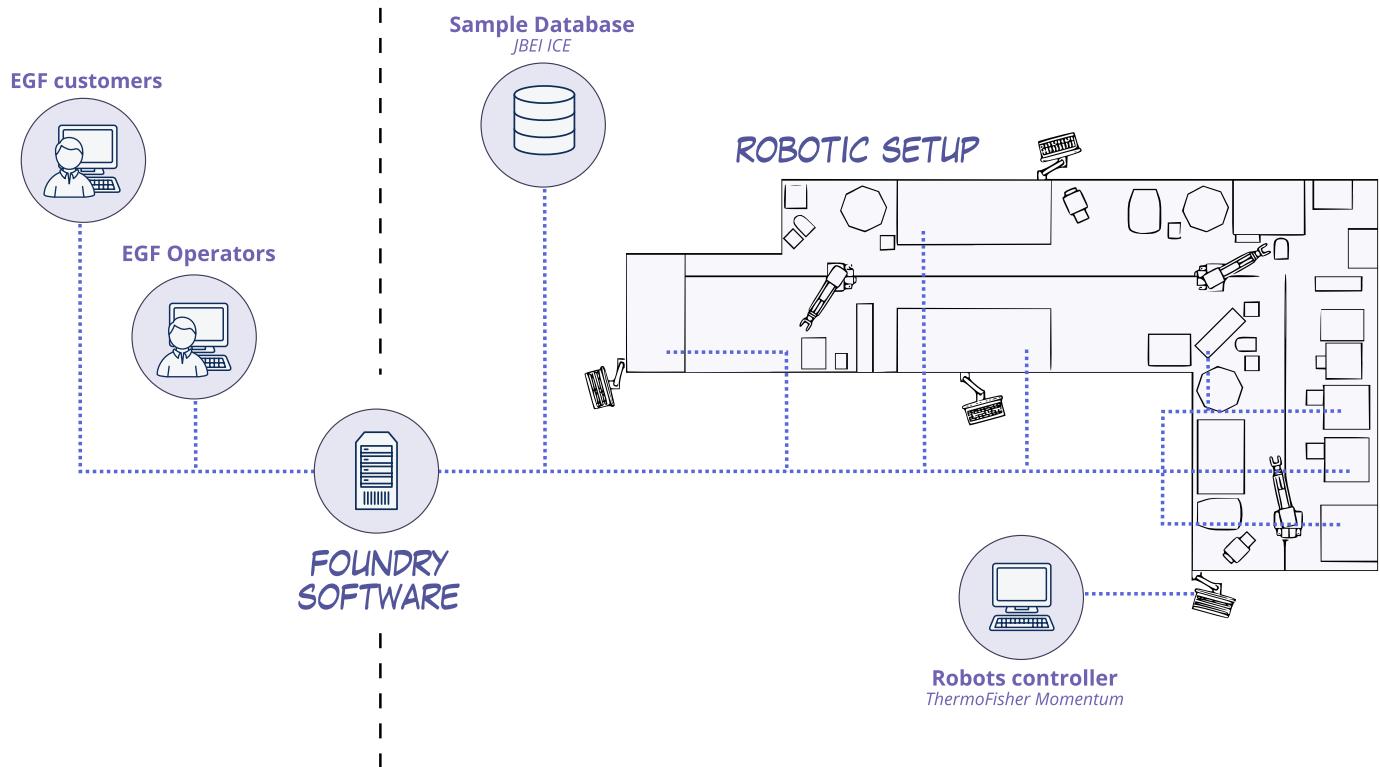
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Order processing at the EGF



customer

Order processing at the EGF

● Current software project ● Future project

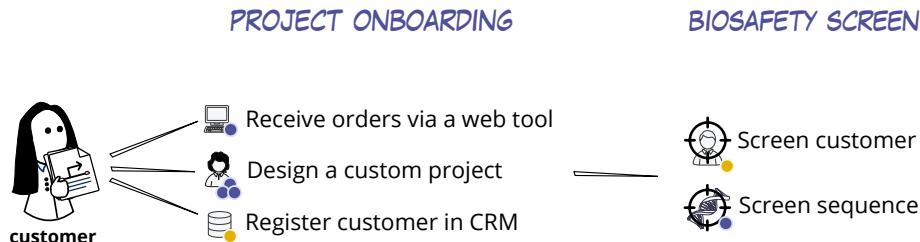
PROJECT ONBOARDING



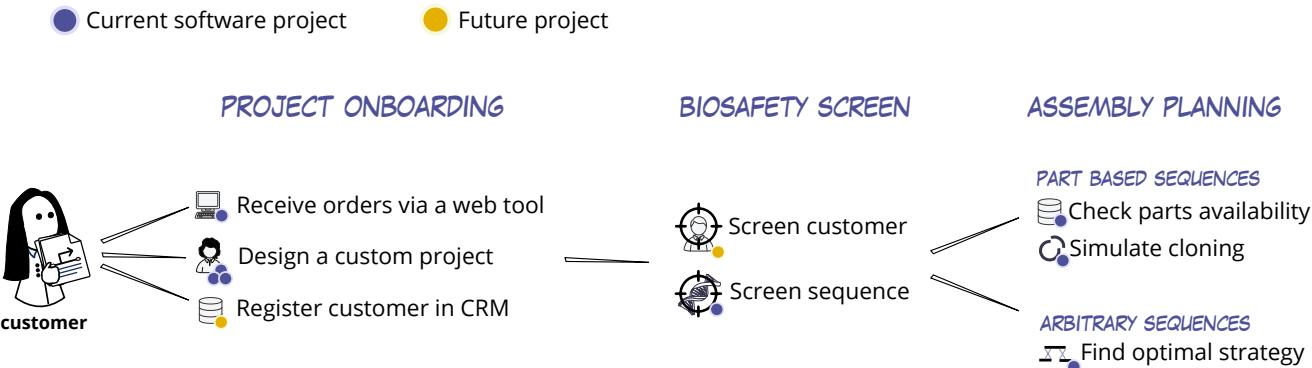
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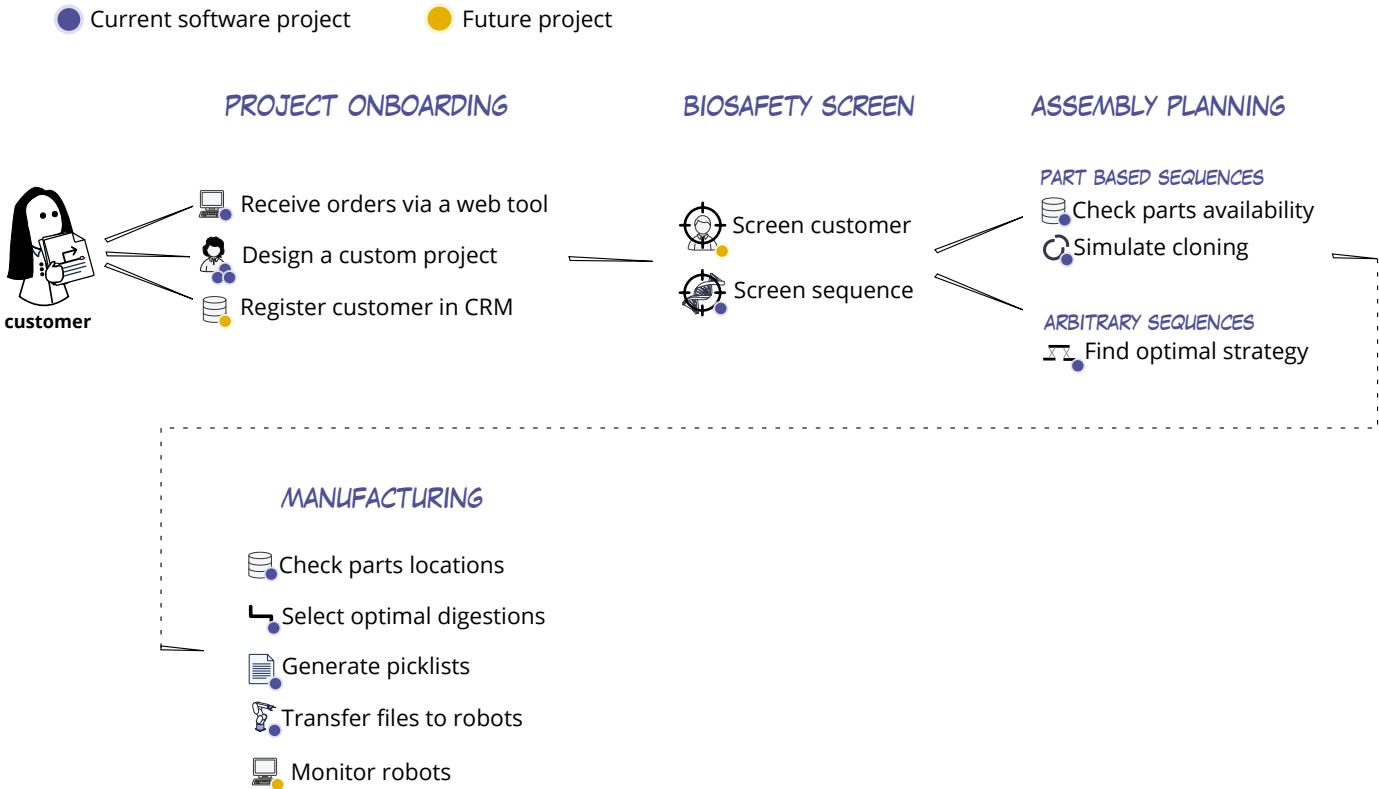
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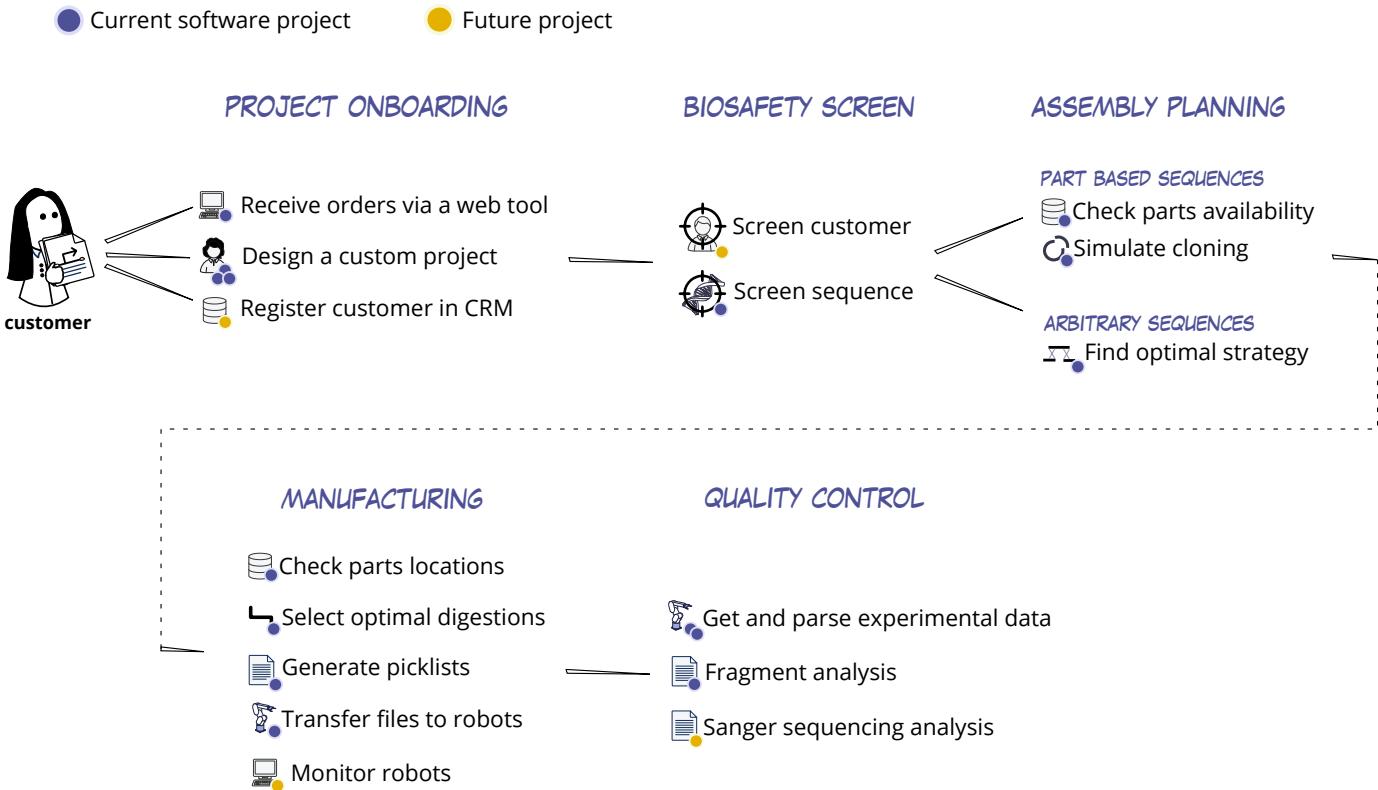
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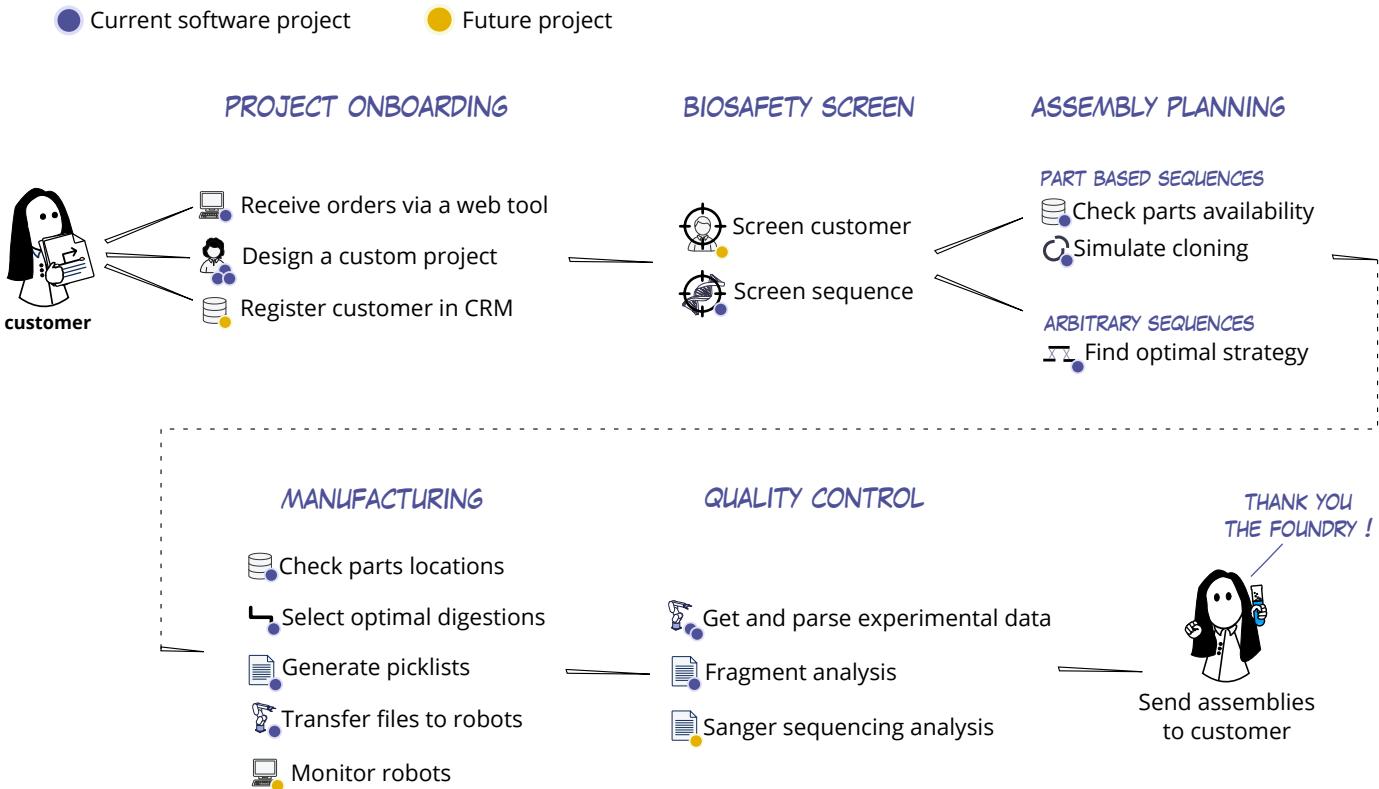
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- ▶ **Look out for what you can outsource:** it gets cheaper by the year
- ▶ **Don't order Ebola !** At least not from us
- ▶ **Learn to code:** it will give you biological super-powers



Thank you !