

COllaborative Management Platform for detection and Analyses of (Re-) emerging and foodborne outbreaks in Europe

# A global platform for the sequence-based rapid identification of pathogens

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This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 643476. " research and innovation programme under grant agreement No 643



### Infectious disease situation 2015

- Dynamics of common infectious diseases are changing
  - Demographic change, population density, anti vaccine, AMR, etc.
- New diseases emerge frequently
  - Deforestation, population growth, health system inequalities, travel, trade, climate change
- Effects are difficult to predict due to complexity of problems
  - Rapid flexible response
- Public health and clinical response depend on global capacity for disease surveillance
  - Rapid sharing, comparison and analysis of data from multiple sources and using multiple methodologies





Clinical research response to ID outbreaks usually fragmented and too late







## What the world needs

- Real-time data on occurences of all infectious agents
- (Automatic) detection of related clusters in time and space
- Possibility to observe trends in clones and species as well as virulence and resistance
- Ability to rapidly compare between all types of data

There can be no real-time surveillance without real-time data sharing





## NGS advantages

- Laboratory diagnostics increasingly rely on (pathogen) genomic information
- RNA / DNA are common across pathogens, therefore, methods to analyse pathogen genomes are potentially universal
- Next generation sequencing capacity is developing fast, and costs are becoming competitive
- Capturing NGS developments may provide a universal language that can be harnessed for early detection of outbreaks across disciplines and domains
- If the technology keeps developing, less equipped labs may leapfrog





### Our vision: to build one system that serves all









#### Epidemic preparedness research: European Union-supported efforts

- Prediction
  - Emergence, surveillance, modelling
- Early recognition and containment
  - Surveillance, clinical awareness, infection control
- Data infrastructure
  - Data repositories, sharing
- clinical research
  - pathogen & disease characterisation
  - prevention & treatment
- funding





## **COMPARE** principles

- COMPARE is sector-, domain- and pathogen-independent
- Analyzing sequence-based pathogen data in combination with associated (clinical, epidemiological and other) data
- Building on established infrastructures (ENA, Elixir)
- COMPARE is a **user-driven system**, designed with the information needs of its intended diverse group of future users and other stakeholders in mind
- COMPARE will make **optimal use of existing and future complementary systems, networks and databases,** ensuring compatibility where needed
- COMPARE is a **flexible**, **scalable** and **open-source based** informationsharing platform
- 1 December 2014 31 November 2019





#### **Project structure**





### WP9 Information sharing platform





-02

### Data comparison problem

### Global repositories > 1-1000 Tb data



Client ~1-100 Gb data

Internet ~1Gb/hour

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#### Workpackage 9: Data infrastructure design

- Sharing of highly structured and well-described data
  - COMPARE standards (e.g. checklists relating to isolates)
  - Data reporting tools that support the structuring and validation of data
- Support for a spectrum of data types
  - Raw NGS to assemblies
  - Derived data: typing information, AMR profiles, etc.
- Data availability
  - Early pre-publication private access, where required, for defined user groups according to explicit data-sharing agreements
  - Rapid flow of data to full public availability and global presentation
- Data discovery and retrieval systems, taking full advantage of data and metadata structures
  - Cloud-based autonomous analytical workflows (assembly, typing, phylogenetics, etc.)
  - Unifying data portal







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### **Current status - IT**







The COllaborative Management Platform for detection and Analyses of (Re-) emerging and foodborne outbreaks in Europe is a collaboration of 29 institutions with experience in outbreak detection and response in areas of human health, animal health and food safety.

#### **COMPARE** Reference Genomes

This COMPARE Reference Genomes page offers a curated selection of published reference sequences covering viral, bacterial and protozoan genomes. These sequences can be searched and retrieved via the following URLs as tagged records in the European Nucleotide Archive (ENA). The complete COMPARE Reference Genomes dataset can be retrieved via the following URL:

http://www.ebi.ac.uk/ena/data/xref/search?source=COMPARE-RefGenome

ENA sequence or sample accessions for a single sample/isolate in the dataset can be returned using the following URL:

http://www.ebi.ac.uk/ena/data/xref/search?source=<source>&source\_accession=<source\_accession>

where source\_accession is the isolate/sample name as shown in the table below, for example:

http://www.ebi.ac.uk/ena/data/xref/search?source=COMPARE-RefGenome&source\_accession=Beijing/55028/2007/CHN

The ENA record, shown in the 'Target primary accession' column of the result from the above URL, can be retrieved with the following URL:

http://www.ebi.ac.uk/ena/data/view/<Target\_primary\_accession>

where Target\_primary\_accession has been inserted from the response to the previous URL (e.g. http://www.ebi.ac.uk/ena/data/view/GQ856465).

More extensive functions are described for <u>REST</u> services relating to the COMPARE Reference Genomes. Users should note that records in the dataset are served from ENA and are denoted as belonging to the dataset through ENA <u>cross-reference</u> annotations.

The below table serves as a quick overview of the COMPARE Reference Genomes set with direct hyperlinks to the INSDC records. Text in brackets next to a taxon name represents serovar or genotype information.

Sample/Isolate ID	Aggregated taxonomic name or Taxon name	Genome	INSDC record(s)			
Norwalk/1968/US	NoV/GI.P1/GI.1	complete	M87661			
Southampton/1991/UK	NoV/GI.P2/GI.2	complete	L07418			
NLV/VA98115/1998	NoV/GI.P3/GI.3	partial	AB287450			
Chiba407/198/JP	NoV/GI.P4/GI.4	complete	AB042808			
Musgrove/1989/UK	NoV/GI.P5/GI.5	partial	AJ277614			
BS5/1997/DE	NoV/GI.P6/GI.6	complete	AF093797			

#### **Reference genomes**

- Curated selection of published reference sequences covering viruses, bacteria and protozoa
- Summary page and entry point at http://www.ebi.ac.uk/ena/about/com pare-reference-genomes
- Searchable through webservices
- Launched 18.6.15, extended 25.8.15

#### In progress Protocols for sampling and handling Ongoing benchmarking and ring trials





#### **COMPARE** data hubs

- On-request service to share pre-publication data
  - Set up: provider, consumer accounts, scope, etc.
  - Providers report data through existing COMPARE interfaces
  - Consumers retrieve metadata (web or spreadsheet manifest) and data (Globus FTP)
- Several existing hubs, including
  - dcc\_sibelius, for the Influenza H5N8 pilot pre-publication read data and metadata
  - dcc\_compare, for replication of overall COMPARE public content, e.g. for external clouds or other infrastructure; currently all bacteria, viruses and some parasites, in time refinements expected







### **Cloud compute**

- Embassy environment
  - Available to COMPARE
    - OpenStack framework (in place)
    - BioLinux standard machine (in place)
  - In development
    - CGE Docker
    - Discussions with CLIMB, NECTAR, IFB-Cloud (Galaxy)
- Development of analysis workflows
  - Evergreen
  - Assembly (Velvet + Prokka)
  - Metagenomics
  - CGE
  - iPython environment for engagement of workflow environments





### Bacterial Analytic Pipeline







### **User Statistics**



#### Until now: >175,000 submissions From + 8,000 IP-adresses

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1			Attribute Description									
2	Field Name	Mandatory	Description									
3	sample_name	No	The name of the isolate the user uses to identify the sample									
4	group_name	Not Yet Used	The name of the group. Adding a group name will incorporate the sample in the analysis pipeline execution of that group									
5	file_names	Yes	Name of all files associated to this sample. Multiple filenames should be seperated by a space									
6	sequencing_platform	Yes	Choose between: LS454, Illumina, Ion Torrent, ABI SOLiD and unknown									
7	sequencing_type	Yes	Choose between: single, paired, mate-paired, and unknown									
8	pre_assembled	Yes	Has the uploaded sample data been assembled? yes / no									
9	sample_type	Yes	Choose between:isolate ormetagenomic									
10	organism	Yes	Write 'unknown' if the organism name is unknown									
11	strain	No	Strain type ID									
12	subtype	No	Subspecific genetic linage, i.e MLST, serovar and biotype									
13	country	Yes										
14	region	No				=						
15	city	(No)										
16	zip_code	(No)	Please provide as much information as possible. Low resolution locations reduce the usability. The									
17	longitude	(No)	minimal recommended option is to provide either city, zip_code or longitude and latitude coordinates.									
18	latitude	(110)										
19	location_note	No	Additional relevant details about the location									
20	isolation_source	Yes	The flost from which use sampler sould be has been dated. This should be a proper scientific name of one									
21	source_note	No	Additional relevant details about the isolation source. i.e. blood, laboratory experiment or urine									
22	pathogenic	Yes	Is the organism decreed pathogenic? yes / no / unknown									
23	pathogenicity_note	No	Additional relevant details about the organism's pathogenicity									
24	collection_date	Yes	The date of the sample collection. Use one of the following format: YYYY-MM-DD or YYYY-MM or YYYYY									
25	collected_by	No	Name of the institute or person who took the sample									
26	usage_restrictions	Yes	Choose either 'private' or 'public'. Note that private data will be deleted after some time to free disk space on the server.									
27	release_date	Not Yet Used	Write the date from when the data and results should be public available. Format: YYYY-MM-DD									
28	email_address	Not Yet Used	Email adress of the uploader									
29	notes	No	Any additional information can be added									
30	insert_size	Yes	The insert size must be given as an integer (i.e. no decimals)									
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6	Escherichi C696-12	2 genes=eael	Denmark			None	None		human	yes		201	2	397	5437311	78570	Escherichieco	oli[ST-2 e	coli[ADK·NA		as	tA,celb,(Ir	ncFIB(AP	ColRNAI,C	IncF[F-:A-	NA	NA		
7	Escherichi C697-12	2A genes=eae l	Denmark			None	None		human	yes		201	2	218	5214489	103647	Escherichieco	oli[ST-1 e	coli[ADK-NA		as	tA,eae,e Ir	ncFII,Incl	FIB(AP0019	IncF[F23:	NA	NA		
8	Escherichi C697-12	2B genes=eae (	Denmark			None	None		human	yes		201	2	233	5210364	96034	Escherichieco	oli[ST-1 e	coli[ADK·NA		as	tA,eae,e Ir	ncFII,Inci	FIB(APO019	IncF[F23:	• NA	NA		
9	Escherichi C748-12	2 genes=vtx: [	Denmark			None	None		human	yes		201	2	279	5363379	83509	Escherichieco	oli[ST-2 e	coli[ADK-NA		ce	b,ehxA, Ir	ncFIA,Inc	IncB/O/K/	IncF[F25*	NA	NA		
10	Escherichi C749-12	2 genes=vtx:1	Denmark			None	None		human	yes		201	2	147	4905062	116559	Escherichieco	oli[Unkre	coli[ADK·NA		cd	tB,espP, Ir	ncFII(pSE	E11),IncFIB(	IncF[F74*	NA	NA		
11	Escherichi C751-1	genes=vtx.l	Denmark			None	None		human	yes		201	2	396	5255403	35/91	Escherichieco	oli[Unkre	CONTADK-NA	eul2	en	xA,espi, ir a iroN is Ir		CINCB/U/K/	IncE[E6*:		NA		
13	Escherichi C659-12	2 genes=vtx1	Denmark			None	None		human	ves		201	2	441	5000054	26095	unknown eco	oli[ST-5 e	coli[ADK-NA	aadA	A1 dfr as	tA iha p Ir	ncFII(pRS	S Col(BS512	IncF[F25*	NA	NA		
14	Escherichi C757-12	2 genes=eael	Denmark			None	None		human	yes		201	2	429	5170629	29561	unknown eco	oli[ST-1 e	coli[ADK-NA		cif	,eae,efa Ir	ncl1,IncF	B(AP0019	IncF[F-:A-	NA	NA		
15	Escherichi C760-12	2 genes=vtx: [	Denmark			None	None		human	yes		201	2	253	5005040	43519	Escherichieco	oli[ST-5 e	ecoli[ADK·NA	blaT	EM-1E as	tA,celb,i Ir	ncFII(pRS	S Col(BS512	IncF[F25*	NA	NA		
16	Escherichi C767-12	2 genes=;ML	Denmark			None	None		human	yes		201	2	313	5288716	48840	Escherichi eco	oli[ST-8 e	coli[ADK-NA		ce	b,gad,il Ir	ncFII(29)	, Col(MG82	IncF[F16*	NA	NA		
17	Escherichi C770-12	2 genes=vtx: [	Denmark			None	None		human	yes		201	2	544	5501587	22843	unknown eco	oli[ST-7 e	coli[ADK-NA		as	tA,iha,ir Ir	ncFII(29)	Col(MP18	IncF[F35*	NA	NA		
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20	Escherichi C812-1	2 genes=eael	Denmark			None	None		human	yes		201	2	225	5157068	124133	Escherichieco	oli[ST-3 e	CONTADK-NA		as	tA,eae,e ir tA cif ea ir	ncFII,Incl	LDCB/O/K/	IncE[E_:A	NA NA	NA		
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22	Escherichi C819-12	2 genes=eael	Denmark			None	None		human	ves		201	2	212	5259174	144767	Escherichieco	oli[ST-1 e	coli[ADK-NA		as	tA,eae,e Ir	ncFII,Incl	FCoIRNAI	IncF[F23:	NA	NA		
23	Escherichi C820-12	2 genes=eael	Denmark			None	None		human	yes		201	2	277	5436245	79411	Escherichieco	oli[ST-2 e	coli[ADK·NA		as	tA,cba,c Ir	ncl1,IncF	B(APO019	Incl1[Unk	NA	NA		
24	Escherich C821-12	2 genes=eae l	Denmark			None	None		human	yes		201	2	260	5235519	115457	Escherichi eco	oli[ST-6 e	coli[ADK-NA		as	tA,eae,e Ir	ncl1,IncF	IncB/O/K/	IncF[F-:A-	NA	NA		
25	Escherich C849-12	2 genes=eae (	Denmark			None	None		human	yes		201	2	220	5245766	126677	Escherichieco	oli[ST-1 e	coli[ADK-NA		as	tA,eae,e Ir	ncFII,Incl	FCoIRNAI	IncF[F23:	<sup>A</sup> NA	NA		
26	Morganel C848-12	2 genes=;ML	Denmark			None	None		human	yes		201	2	52	4055781	176604	NA eco	oli[Unkre	coli[ADK·NA				510/40	001010	NA	NA	NA		1
27	Escherichi C850-12	2 genes=eael	Denmark			None	None		human	yes		201	2	254	5065655	81376	Escherichieco	oli[ST-1 e	COTILADK NA		as	tA,cif,ea ir	ncFIB(AP	001918)	IncF[F-:A-	NA NA	NA		
20	Escherichi C852-12	genes=eael	Denmark			None	None		human	ves		201	2	243	5375983	90792	Escherichieco	oli[ST-3 e	coli[ADK-NA		as	tA cif ea Ir	ncFIB(AP)	(IncY IncB/	IncE[E-:A-	NA	NA		
30	Escherichi C874-12	2 genes=vtx:1	Denmark			None	None		human	yes		201	2	287	5474038	97468	Escherichieco	oli[ST-4 e	coli[ADK-NA		eh	xA,gad,i Ir	ncFIB(AP	(Col156,Co	IncF[F25*	NA	NA		
31	Escherichi C884-12	2 genes=eae l	Denmark			None	None		human	yes		201	2	200	5155599	121342	Escherichi eco	oli[ST-3 e	coli[ADK NA		as	tA,cif,ea Ir	ncFIB(AP	(IncB/O/K/	IncF[F-:A-	NA	NA		
32	Escherichi C885-12	2A genes=eae l	Denmark			None	None		human	yes		201	2	115	4755036	103805	Escherichi eco	oli[ST-4 e	coli[ADK·NA		cif	,eae,espA	,espF,esp	col156	NA	NA	NA		
33	Escherichi C885-12	2B genes=eae (	Denmark			None	None		human	yes		201	2	240	5253067	72400	Escherichieco	oli[ST-3 e	coli[ADK·NA		as	tA,eae,e Ir	ncFIA(HI1	1Col156	IncF[F5:A	NA	NA		
34	Escherichi C886-12	2 genes=eael	Denmark			None	None		human	yes		201	2	258	5264368	96518	Escherichieco	oli[ST-3 e	coli[ADK NA		as	tA,cif,ea Ir	ncl1,IncF	IncB/O/K/	IncF[F-:A-	NA	NA		
35	Escherichi C887-12	2 genes=;MLI	Denmark			None	None		human	yes		201	2	//	4488/33	153149	NA eco	oli[Unkre	COLLADK NA		ga	d,prfB	e El Le el	CelDNAL	NA	NA	NA		
37	Escherichi (892-1)	genes=edet	Denmark			None	None		human	ves		201	2	145	4939191	102286	Escherichieco	bli[ST-2 e	CONTADK-NA		ds CP	b gad k in	ncFII(nCc		IncE[E128	NA NA	NA		
38	Escherichi C893-12	2 genes=vtx: [	Denmark			None	None		human	ves		201	2	208	5306779	82670	Escherichieco	oli[Unkre	coli[ADK NA		cb	a.cma.e Ir	ncFIB(AP	ColRNAI	IncF[F25*	NA	NA		
39	Escherichi C894-12	2 genes=eae l	Denmark			None	None		human	yes		201	2	206	5277292	94653	Escherichieco	oli[ST-1 e	coli[ADK-NA		as	tA,eae,e Ir	ncFII,Incl	FIB(AP0019	IncF[F23:	NA	NA		
40	Escherichi C895-12	2 genes=vtx: [	Denmark			None	None		human	yes		201	2	185	5204668	85195	Escherichieco	oli[ST-6 e	coli[ADK·NA		ga	d,iha,lp Ir	ncFII(pRS	S Col156	IncF[F1:A	NA	NA		
41	Escherichi C896-12	2A genes=eae [	Denmark			None	None		human	yes		201	2	247	5264467	68277	Escherichieco	oli[ST-3 e	coli[ADK-NA		as	tA,eae,e Ir	ncFIA(HI1	1Col156	IncF[F5:A	E NA	NA		
42	Escherichi C896-12	2B genes=eael	Denmark			None	None		human	yes		201	2	124	4758033	104256	Escherichieco	oli[ST-4 e	coli[ADK·NA		cif	,eae,espA	,espF,esp	r Col156	NA	NA	NA		
43	Escherichi C904-12	2A genes=vtx: [	Denmark			None	None		human	yes		201	2	593	5523711	43914	Escherichieco	oli[ST-6 e	coli[ADK-NA		ce	b,ehxA, Ir	ncFIB(AP	(Col156	IncF[F25*		NA		
44	Escherichi C505-12	genes-edet	Deninark			None	None		numan	yes		201	2	304	5058172	80202	Escherichieco	511[51-1 e	CONTADICINA		as	ua,eae,e ii	iern,inei	FID(APOUIS	incr[r25.	- INA	INA		
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### Current developments - IT

- Ability to create own shared site
- Combining map, phylogeny and analysis (microreact)
- Evergreen trees
- Bring your own tools (already ability for own DB)





### Conclusions

- WGS/NGS is rapidly entering diagnostic and public health arena, with near real-time data generation
- Sequence platforms rapidly developing, cheaper, simpler
- Bottleneck at level of bioinformatics, particularly for intergroup comparison, national, international
- COMPARE aims to develop infrastructure and ICT to meet the coming demand
- In the coming years, we will be seeking partners for pilot projects





## Pilot projects in 2016

- Cross cutting: Escherichia coli, ESBL, norovirus, metagenomics
- Clinical WP: AMR
- Public health WP: 6 food-borne pathogens
- Emerging infections WP: Influenza and MERS CoV
- Ad hoc





### Our vision: one system serves all



#### **Guiding principles:**

- Cross sector, cross domain, open source (not commercial)
- Interaction with the rest of the world (all inclusive)
- Data for action (actionable outputs)
- Central repository (ENA, DDJ, NCBI) (bring the tools to the data)

#### There can be no real-time disease detection & surveillance without real-time data sharing



