AURIA BIOBANK

Hospital Biobank Samples and Data for Real-World Evidence Studies

15.2.2019 Biobanking 2019, Porto

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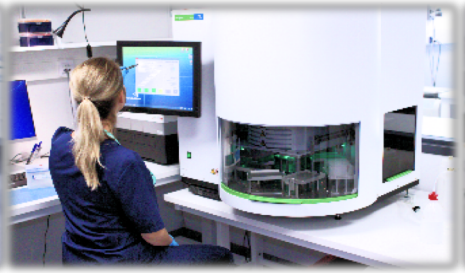
Biobank activities

- Biobanking in Finland
- Auria Biobank: samples, capabilities and services for RWE studies
- Research examples

Biobanks in Finland

- The biobanks' goal is to aid in development of novel treatments and treatment practices, as well as promotion of health by biomedical and health science research
- By combining biological data from samples with clinical data, it is possible to study mechanisms underlying diseases and the relationship of genetics, environment and lifestyle
- Biobank's samples and data can be utilized in development of personalized diagnostics and treatment
- Biobank act 1.9.2013
- Everyone has the right to give biobank consent and participate in research
- The results from biobank studies are returned to biobank

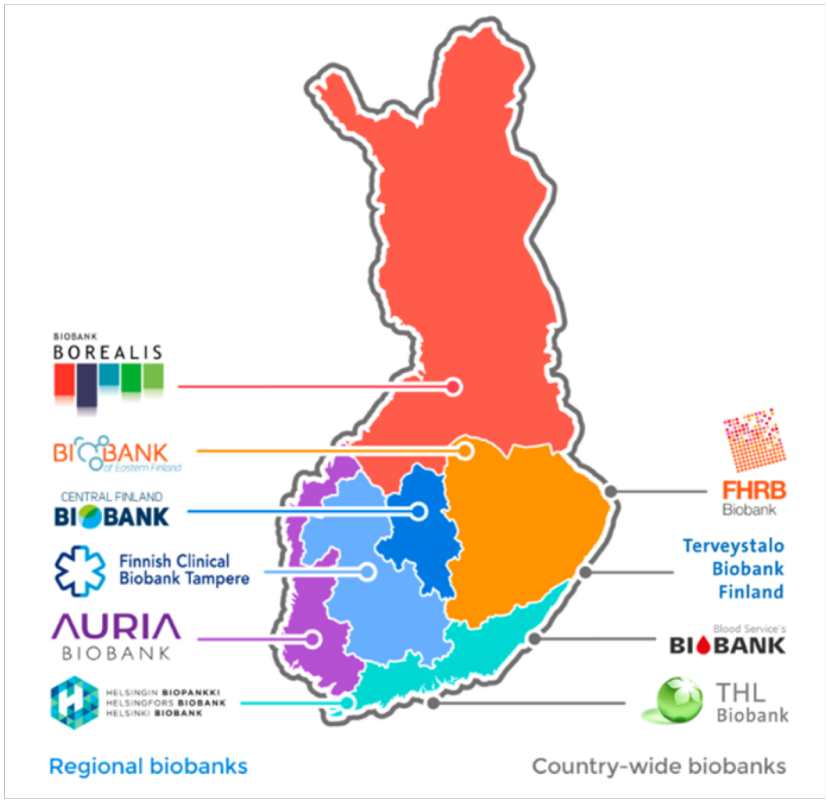
Key advantages of Finnish biobanks

- Homogeneous population, willingness to contribute
- Social security number (Person ID)
- Public health care and national treatment guidelines
- Longitudinal sample collections with associated EHR information
- Hospital-integrated consenting and sample collecting procedures -> resulting in high coverage prospective collections of clinical quality
- Biobank act (1.9.2013) with three important principles
  - *Regulation* by national authorities (professionalism, quality standards)
  - *Protection* of donors' rights (informed consent, privacy protection, sample pseudonymization, right to know in which projects samples have been used)
  - *Promotion* of research and R&D (broad consent, permission to link samples with information from hospital databases and national registries, all raw data from projects should return to biobank for future biobank research purposes)

Finnish Biobanks

Biobank Finland Joint Operator FINBB founded in 2017, domicile Turku

Founders
Helsingin ja Uudenmaan Sairaanhoitopiirin kuntayhtymä
Helsingin yliopisto
Keski-Suomen Sairaanhoitopiirin kuntayhtymä
Jyväskylän yliopisto
Pirkanmaan Sairaanhoitopiirin kuntayhtymä
Tampereen yliopisto
Pohjois-Pohjanmaan Sairaanhoitopiirin kuntayhtymä
Oulun yliopisto
Pohjois-Savon Sairaanhoitopiirin kuntayhtymä
Itä-Suomen yliopisto
Varsinais-Suomen Sairaanhoitopiirin kuntayhtymä
Turun yliopisto



FinBB Cooperative

Aims to serve as a key contributor to making population resources available for advancements in public and personal health
"One-access shop"

Support biobank creators and users in
- providing coordinated services to help biobanks set up infrastructure and processes to create high quality, standardized collections with interoperative utility and critical-mass-based market value
- facilitating scalable, sustainable, revenue-generating utilization of biobank resources by academic, public and commercial biobank users

https://finbb.fi/

FINBB
FinBioBank

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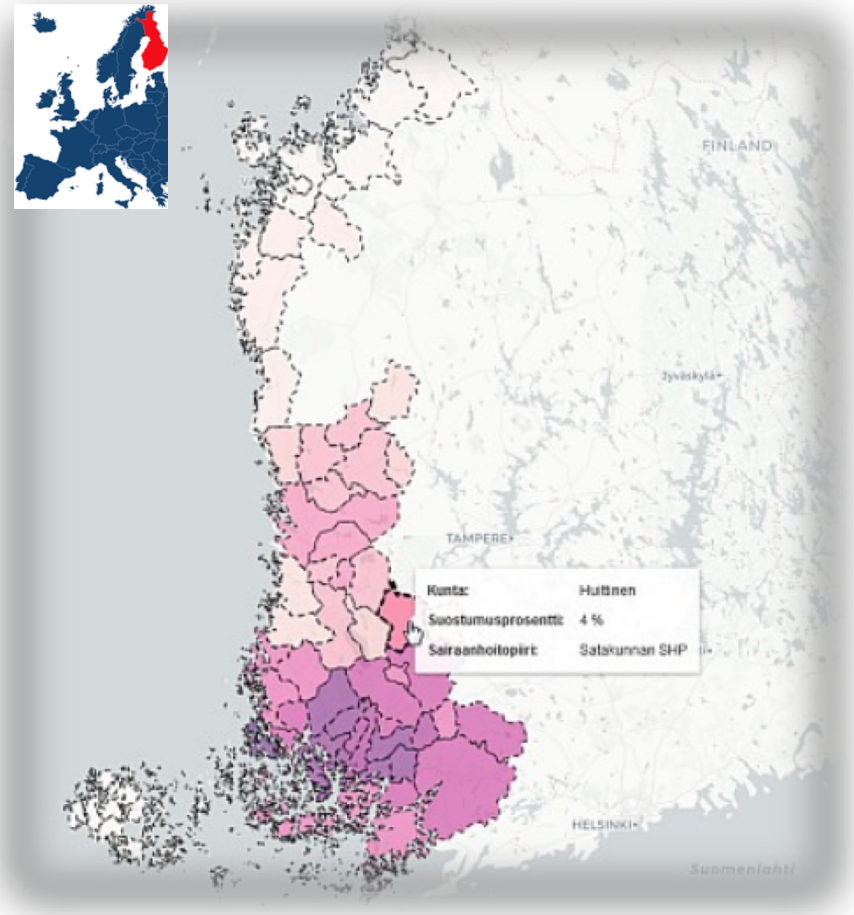
Auria Biobank



- Hospital biobank: Biobank that processes clinical specimens and data in a hospital setting
- A hospital integrated clinical biobank founded in 2012 by the University of Turku and Hospital districts of Southwest Finland, Satakunta and Vaasa
- Authorized to operate in March 2014
- Catchment population ~900 000 people
- A research infrastructure for academic investigators and company R&D
- >160 biobank studies with pharma industry and academic researchers

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Sample collection

- Archive of >1,5 million FFPE samples
  -samples taken before 1.9.2013 transferred to biobank
- Tissue samples (e.g. tumors removed in context with diagnostics or operations)
  -samples 1.9.2013 onwards with a consent
- Blood sample (10 ml EDTA) from every consented patient (TYKSlab, SataDiag, Vaasa) → DNA exctraction
- Feces samples (in collaboration with Microbiota bank)
- Collection of samples for biobank does not compromise normal diagnostics or treatment

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Auria Biobank's services

- Human biological samples (FFPE and frozen tissues, blood, DNA) with related clinical data for biomedical research
- Sample collection and storage, production of tissue microarrays (TMAs)
- Project-based research services
- Real world data and analysis service from clinical data in electronic health records
- Evidence-based feasibility studies and recruitment for clinical trials
- Consultation, advisory and training services related to biobank operations (e.g. protocols, quality systems, contracts and legal aspects, IT systems and registers, operating models)
- Algorithms for data and text mining + algorithm development, digital pathology

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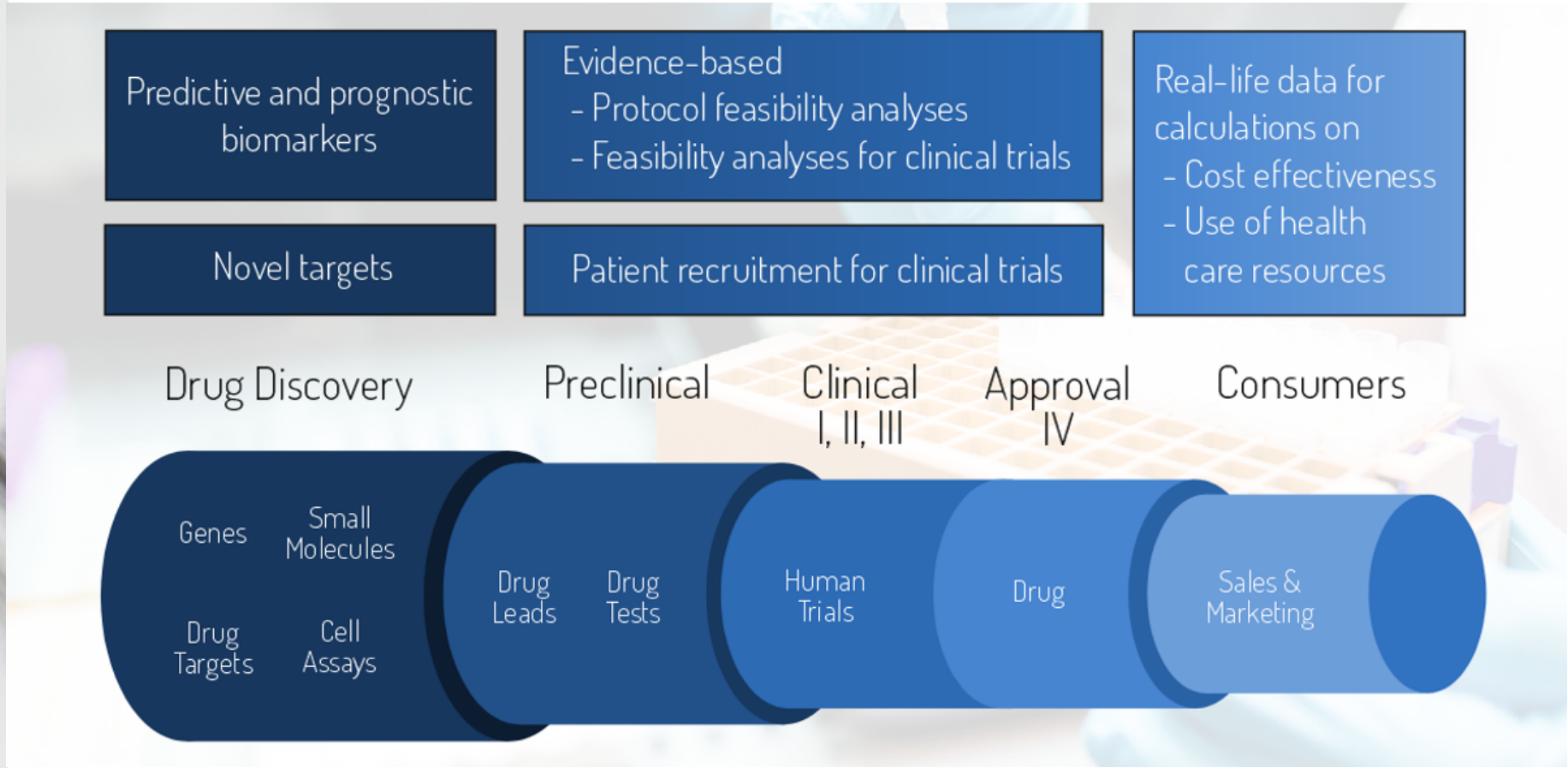
Auria Bio(data)bank in drug development life cycle



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SSTR2A expression in gliomas

www.impactjournals.com/oncotarget/ Oncotarget, 2017, Vol. 8, (No. 30), pp: 49123-49132

Research Paper

Somatostatin receptor 2A in gliomas: Association with oligodendrogliomas and favourable outcome

Aida Kiviniemi[1,2], Maria Gardberg[3], Katri Kivinen[4], Jussi P. Posti[5], Ville Vuorinen[5], Jussi Sipilä[6,7], Melissa Rahi[5], Matti Sankinen[5] and Heikki Minn[8]

- Somatostatin receptor subtype 2A (SSTR2A) is a potential therapeutic target in gliomas
- SSTR2A expression was characterized in 184 glioma samples
  - 101 glioblastomas
  - 23 oligodendrogliomas
  - 60 astrocytomas
- Staining intensity and localization in tumor cells was evaluated and correlated with glioma entities and survival

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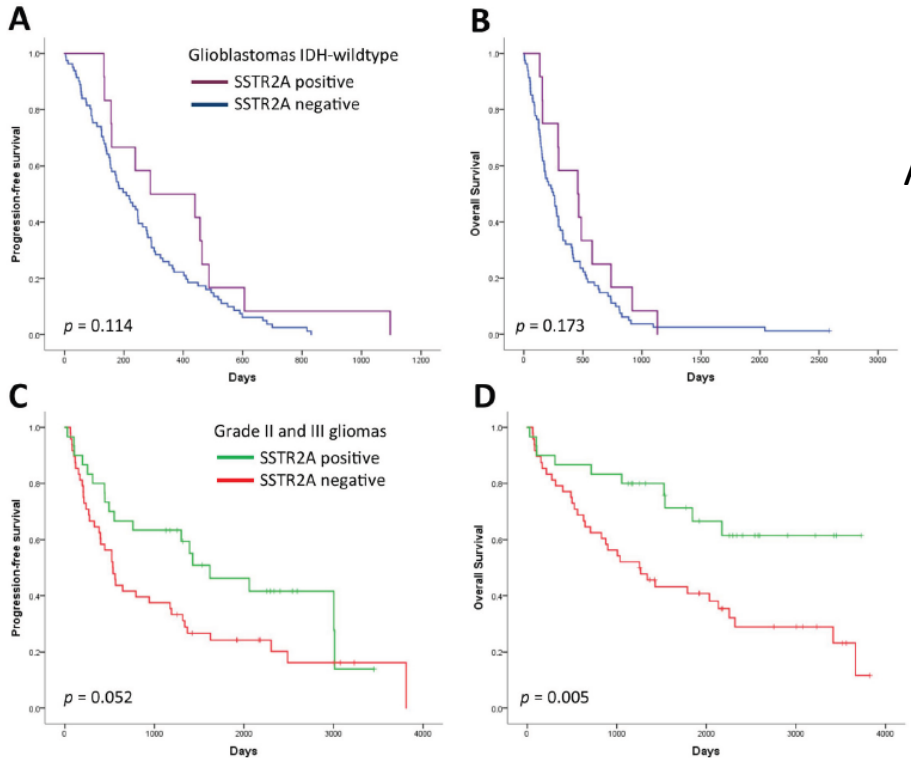
SSTR2A expression in gliomas

SSTR2A expression was found to be infrequent in astrocytomas and
negative in the majority of glioblastomas → no prognostic significance
In oligodendrogliomas, intense membranous and cytoplasmic SSTR2A expression,
positive SSTR2 was related to longer overall survival in grade II and III gliomas
→ potential diagnostic, prognostic and therapeutic value



A, B glioblastomas

C, D grade II–III gliomas

Progression-free survival and overall survival according to SSTR2A status

Kiviniemi *et al*. 2017 Oncotarget, Vol. 8, 49123-49132

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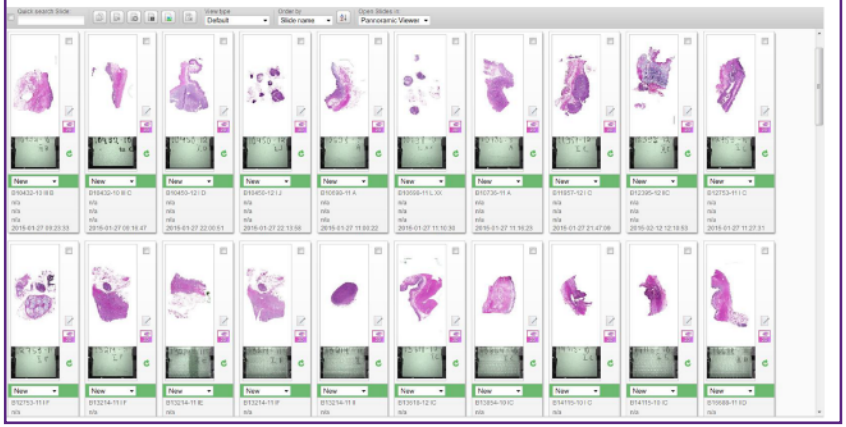
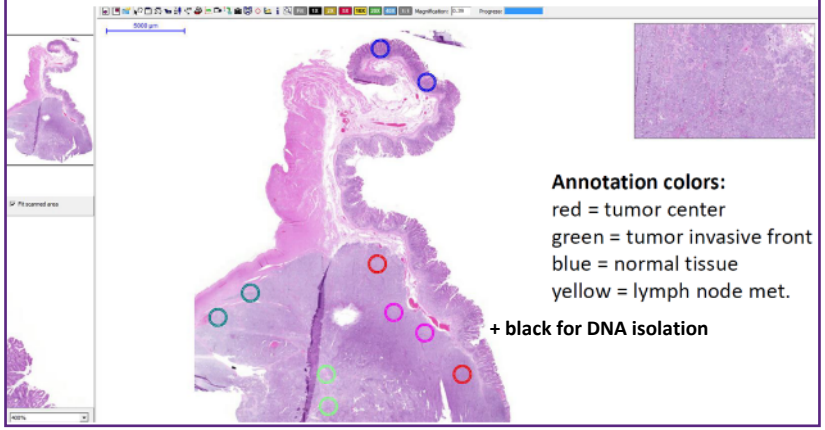
Digipathology for drug discovery

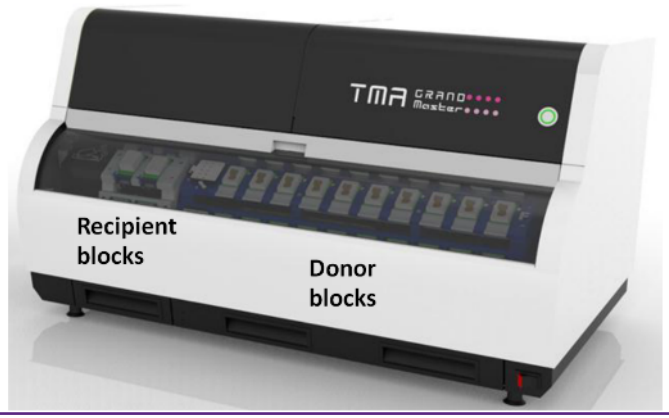
1. Select and scan tissue specimens into web portal



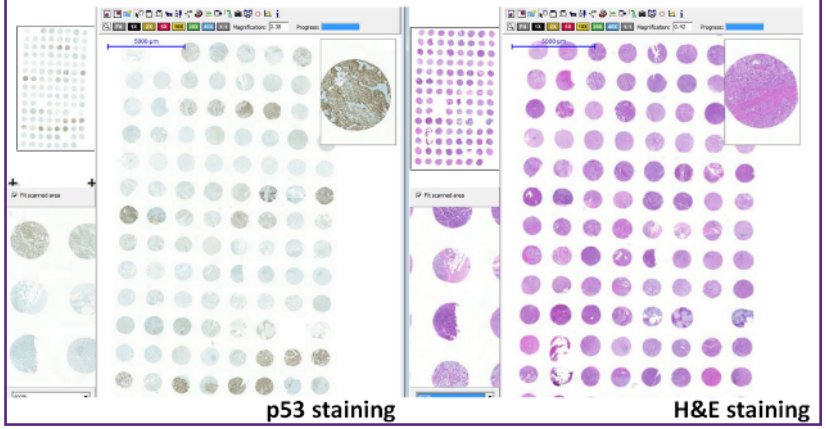
2. Annotate digital slides with regions of interest



3. Construct TMA using automated TMA instrument



4. Stain, scan, study, and score finished TMA blocks



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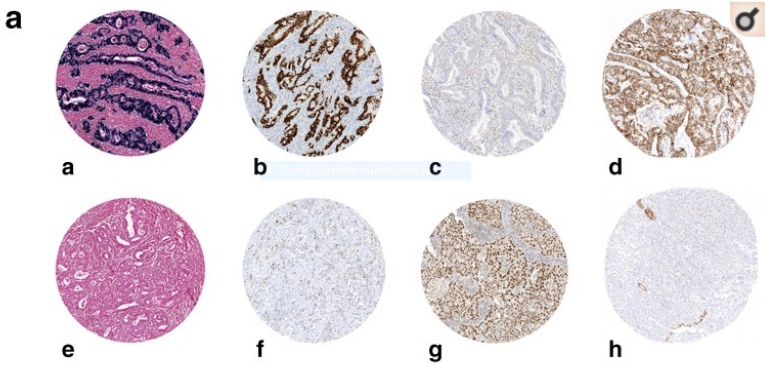
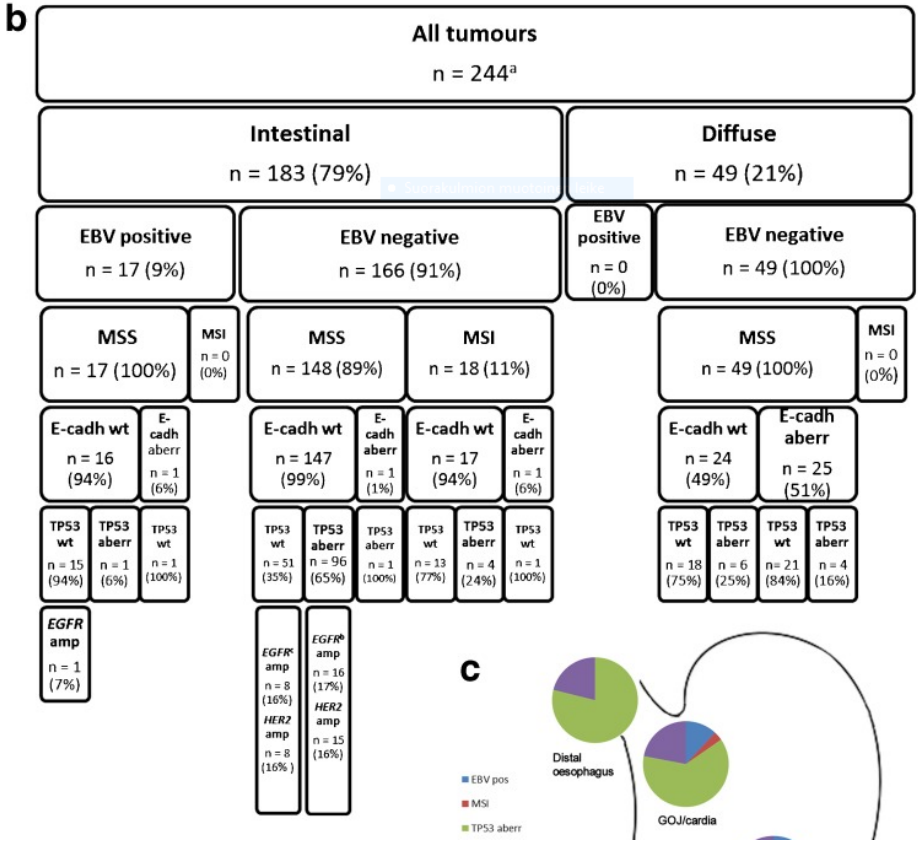
Tissue microarrays and digipathology

TMA	Disease	Patients (#)	Years	Blocks (#)	Cylinders/patient (#)
Prostate cancer	Removal of prostate due to adenocarcinoma	222	2004-2010	18	2 from the core of tumour
Pancreatic cancer	Pancreatic adenocarcinoma	40	1993-2012	2	2 from the core of tumour
Gastric cancer	Intestinal-type adenoca of the stomach, gastro-esophageal junction or distal esophagus	~200	1993-2012	12	2 from the core and 2 from invasive front
Colorectal cancer	Stage II colorectal cancer	250	2005-2012	11	2 from the core and 2 from invasive front
Glioma	Glioblastoma and diffuse glioma	~200	2005-2013	5	2 from the core of tumour
Lung cancer	Non-small cell lung cancer	~500	1993-2013	27	1-2 from the core and from invasive front
Breast cancer	Breast cancer (triple negative)	~200	1998-2012	10	2 cylinders from the core of tumour, metastatic lymph node or inflamed area
Ovarian cancer I	Ovarian granulosa cell tumors	44	1993-2013	2	4 cylinders from the core of the tumor
Ovarian cancer II	High-grade serous ovarian carcinoma	~400	1994-2007	12	2 cylinders from the core of the tumour
Vulvar cancer	Precancerous lesions and primary tumors of vulva, metastatic lymph nodes	140	1999-2013	4	2 from the core and 2 from invasive front; 2 from LSA; 2 from metastatic lymph nodes
Gastrointestinal stromal tumor	Gastrointestinal stromal tumor (GIST)	~100	1993-2016	4	1-2 cylinders / tumor
Head and neck cancer	Squamous cell carcinoma (head and neck and salivary gland cancer)	~400	2004-2015	11	2 cylinders from the core of the tumour, 2 from the invasive front, 2 from metastatic lymph nodes (2 cores from stroma)
cSCC	Squamous cell carcinoma, actinic keratosis and Cutaneous squamous cell carcinoma (cSCC) (skin) Patient with metastasis and without metastasis	64+15	1994-2013	3+2	Cylinders from the tumour, cylinders from the normal tissue
Breast cancer	Infiltrating ductal carcinoma (Her2 negative)	~200	2003-2006	3	1 cylinder / tumor
Lung cancer	Biomarkers in lung carsinoid tumours (NETs)	36	1990-2013	2	Tumor, border, bening lung, bronchus, metastasis
Pediatric	Carsinoma samples from children (kidney, brain/meninges, sarcoma, lymphoma/leukemia, thyroid, others)	57	1993-2012	6	1-2 core from tumor 1-2 core from control
Adenomyosis	Adenomyosis samples	~140	2012-2016	12	1-2 core from adenomyosis 1-2 core from myometrium 1-2 core from myometrium

Case gastric cancer

Gastric cancer: immunohistochemical classification of molecular subtypes and their association with clinicopathological characteristics. *Birkman et al. Virchows Arch. 2018; 472: 369–382*.





- A tissue microarray (TMA) was collected from about **300 gastric cancers** diagnosed and treated at Turku University Hospital between years 1993-2012 and constructed at Auria biobank.
- In situ hybridization for detection of **EBV infection**, IHC staining of P53 for **chromosomally instable subtype** and MSI markers MLH1, MSH2, MSH6 and PMS2 for **microsatellite-instability subtype**.

Gastric adenocarcinomas can be classified into biologically and clinically different subgroups by using a simple method applicable for clinical diagnostics and research purposes

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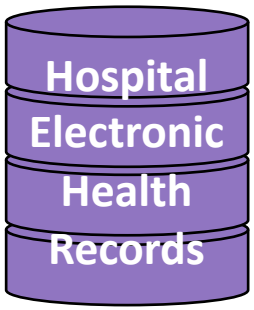
Real-world data linked to samples

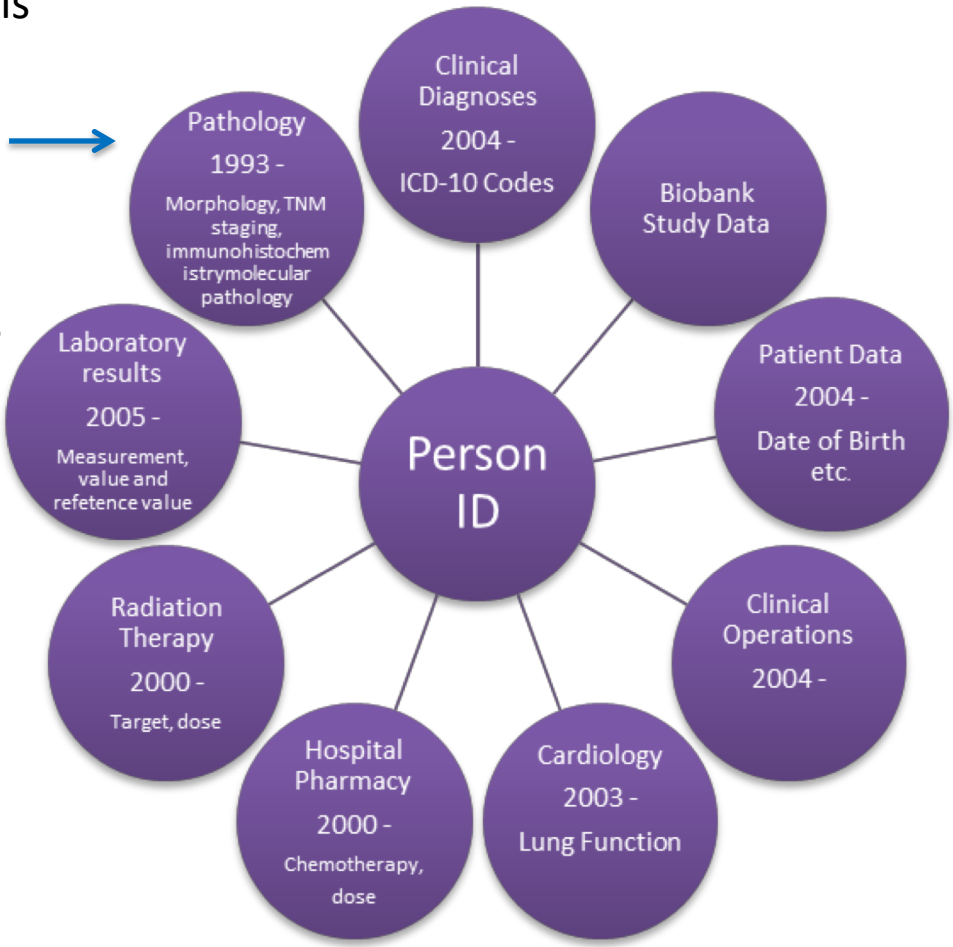
Real-world data: Clinical patient data that is generated in health care outside clinical trials



Clinical data in data lake

National registers
Biobank studies

Auria Biobank's sample and data register



- Longitudinal information on the course of disease, diagnostic tests, operations, response to treatments, outcome etc.
- In electronic format ~2004 onwards
- Possible to combine hospital EHRs with biobank specimens

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Real world data analyses

- Real-life evidence
  - Clinical diagnosis and incidence in Turku University Hospital region
  - Prognosis and status of patients
  - Risk factors
  - Laboratory measurements, treatments
  - Comorbidities
  - Use of hospital resources (number of inpatient periods and length in days per patient and per patient year, number of outpatient visits, operations)
  - Overall survival
- To understand the market (drug use and efficacy, reimbursement decisions)
- To help hospital management, authorities and pharma companies in cost-benefit analyses

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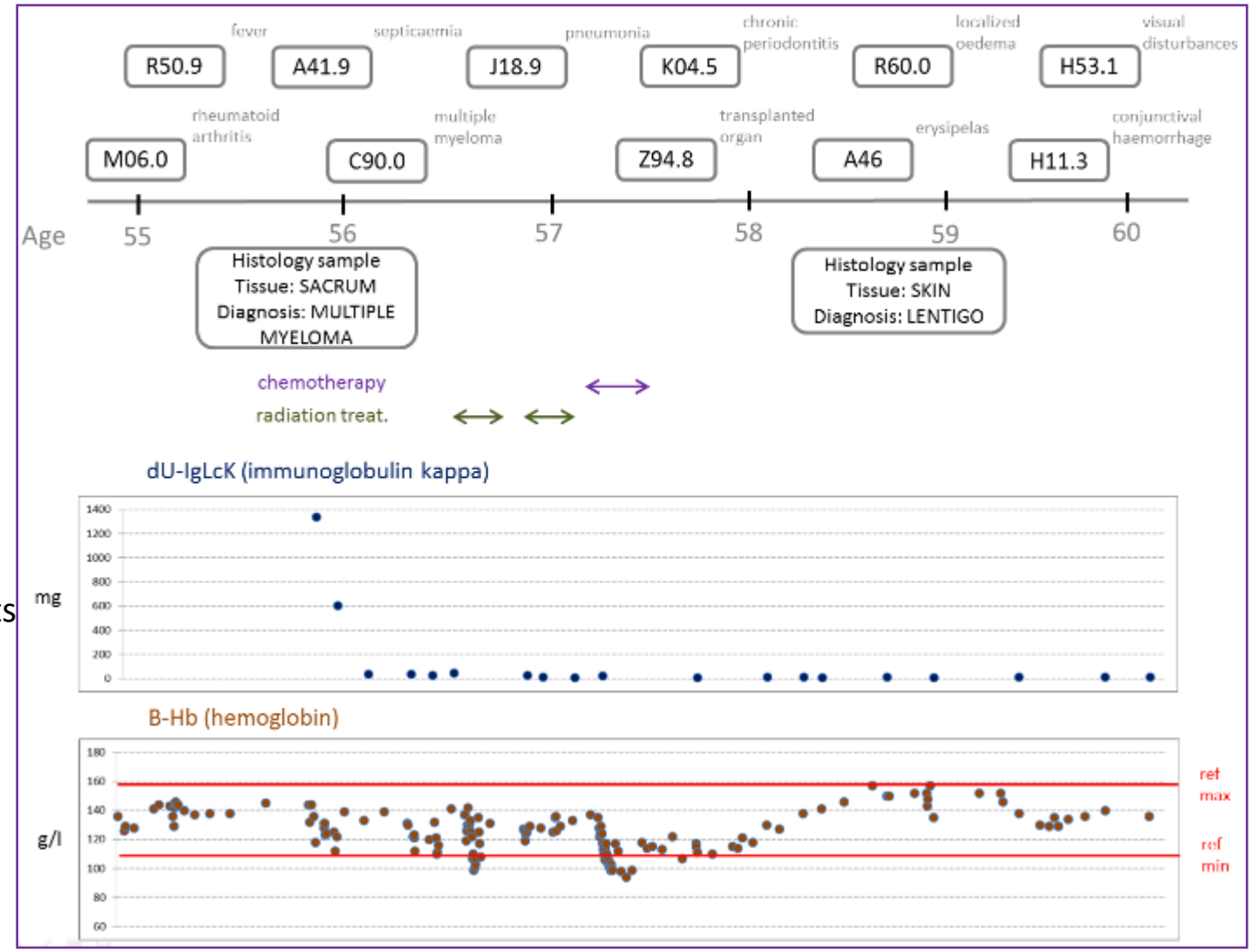
Digital timeline of a patient

Clinical diagnoses

Pathology specimens

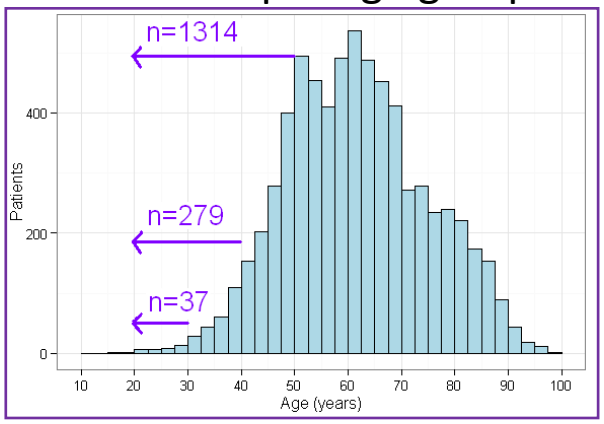
Oncology treatments

Laboratory measurements

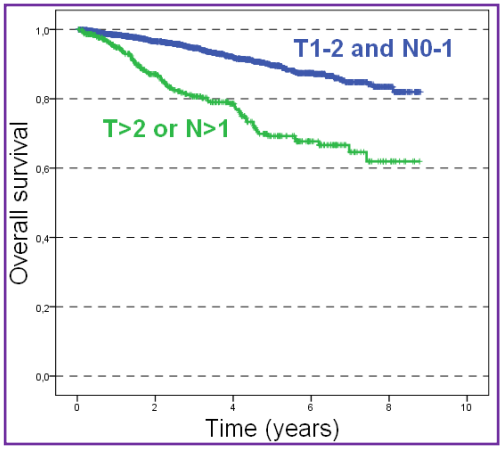


Breast cancer patients at Turku University Hospital

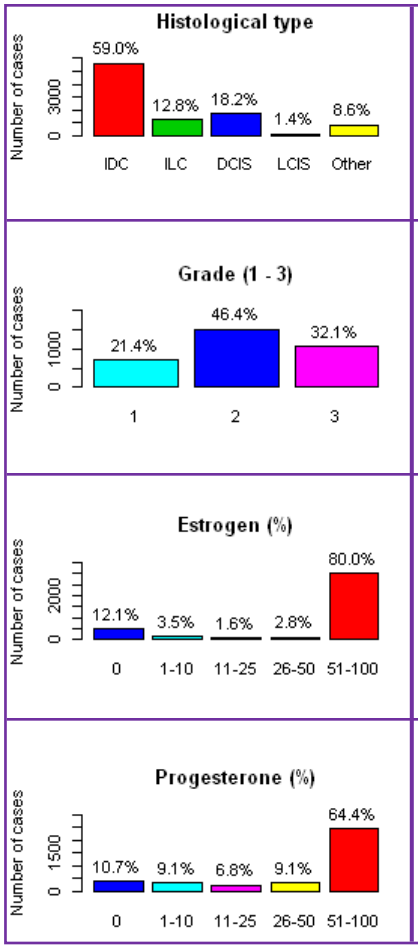
Number per age group



Overall survival



All cases



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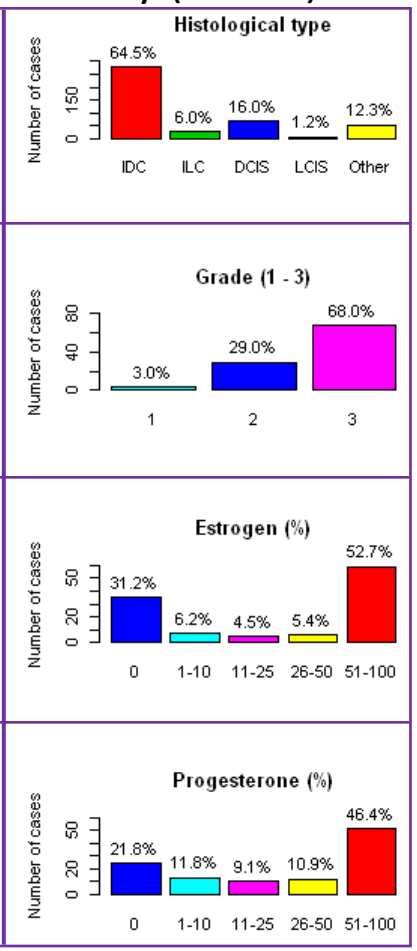
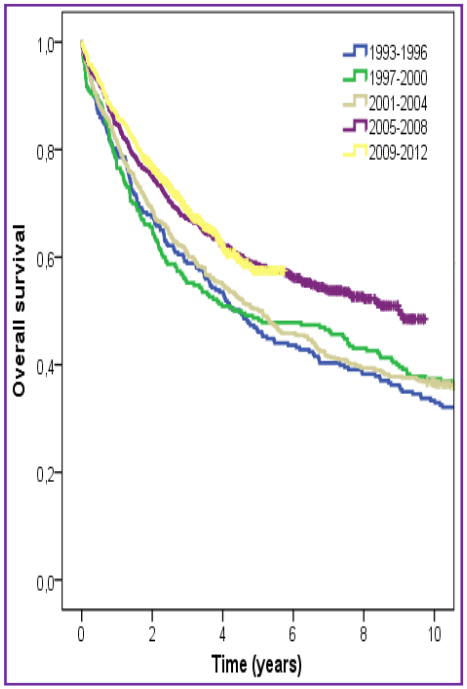


Biobank supporting diagnostics and treatment

Major improvement in survival of CRC patients was observed in 2004, at the time of

- centralization of rectal cancer surgery
- introduction of multidisciplinary teams
- higher number of lymph nodes examined
- implementation of preoperative radiotherapy in rectal cancer
- the use of adjuvant chemotherapy in stage III CRC became also slightly more frequent



The clinical presentation of CRC has remained essentially the same between years 2001 and 2012.

The observed changes have resulted in improved survival in CRC and a marked decrease of non-operable rectal cancer.

Trends in presentation, treatment and survival of 1777 patients with colorectal cancer over a decade: a Biobank study. Heervä E *et al*. Acta Oncol. 2017 Dec 23:1-8.

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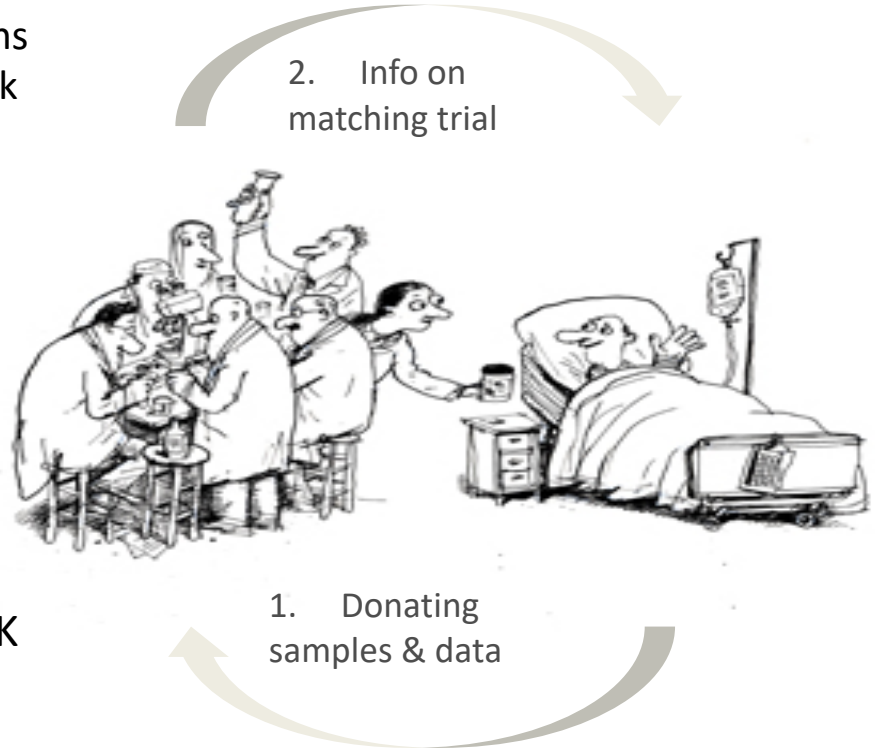
Feasibility studies

Auria projects – clinical trial feasibility & molecular-based patient recruitment

- A series of clinical trials across several indications were simulated in the database of Auria biobank to optimize the future clinical trial protocol.
- Trial feasibility analysis: Auria identified several potential participants for these trials.
- Ethics Committee approved wording to reach out to biobank donors (who had consented to this recontact option).
- Letters were send out to local patients.



Realizing the vision of molecular medicine:
→ From the bed to the benchside AND BACK
→ Offering novel opportunity for patients

Courtesy of Dr. Arndt Schmitz, Senior Technology Expert @ IT Business Partnering Research, Bayer AG

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Challenge of free text

- Majority of clinical data is not yet in structured form
- Mining of relevant information from among big data
- Modification of data in a form that is easy to analyze

- Important example: in case of lung cancer the **smoking status** / history of the patient is highly relevant
- Not in structured form - needs to be mined from unstructured reports
- Only a very small part of the document is relevant for the question (smoking)

xx.xx.xxxx

Tulosyy: Tulee X:n lähetteellä syvän laskimotrombin ja keuhkoembolia epäilyn vuoksi.

Esitiedot

xx-v. nainen, jolla hypertensio, papillaarinen kilpirauhassyöpä oper v. xxxx. Suonikohjuja oper. v. xxxx ja v. xxxx. Nivelrikkoa polvissa, oik. polvi protetisoitu pvmxxxx. Pinnallinen laskimotukos ollut vas. pohkeessa v. xxxx synnytyksen jälkeen.

N. 1 vkon ajan huomannut hengenahdistusta ja sydän tykyttänyt ajoittain. Ajatteli tämän johtuvan kilpirauhasesta, pvmxxx katsottu TSH ja T4v, jotka potilaan aiempaa tasoa. pvmxxx alkoi vas. pohje kipeytyä, jonka vuoksi hakeutui lääkäriin. Tehty vas. alaraajalaskimoiden uä, jossa todettu vasemmalla popliteatason ja pohkeen syvä laskimotromboosi. Oireiston perusteella epäilty keuhkoemboliaa ja lähetetty TYKSiin.

Ei HRT käytössä, silloin tällöin paikallisvalmisteena Vagifem, **tupakoi epäsäännöllisesti 1-2 savuketta/vrk,** suvussa xxxx ollut laskimotrombi ja keuhkoembolia, ei immobilisaatiota, ei leikkauksia viime aikoina.

Lääkitys: Thyroxin 0.1 mg 1.5x1, Atacand plus 1x1, Ideos 1x2

Nykytila: Yt hyvä, RR 160/83, p. 70, tax 36.8, saO2 98, sydämestä ausk. tas. sään. rytmi n. 80/min, mahdollisesti systolinen sivuääni? Pulm. ausk. symm. puhtaat hä:t, hf 12/min. Vatsa palp. pehmeä, myötäävä, aristamaton. Vas. pohje oikeaa turvonneempi, vas. jalassa pitting-ödeemaa puoleen sääreen asti, oik. puolella ei turvotusta. ADP +/+. Jalkojen iho terve.

-> Development of algorithms for text mining

Auria participates in FinnGen

- The FinnGen research project is an academic industrial collaboration aiming to identify genotype-phenotype correlations in the Finnish founder population.
- The project aims to produce close to complete genome variant data of 500 000 biobank participants using GWAS genotyping.
- The GWAS data are combined with phenotype data produced from several national health registries (longitudinal follow-up data).
- The genome data created in connection with the research will immediately be available for researchers involved in the project
- The data will be returned and stored once a year to the biobank from where the sample was delivered to be available for other biobank studies (data on 3600 patients will be available at Auria 9/2019).

FINNGEN

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Biobanks and real world data analyses

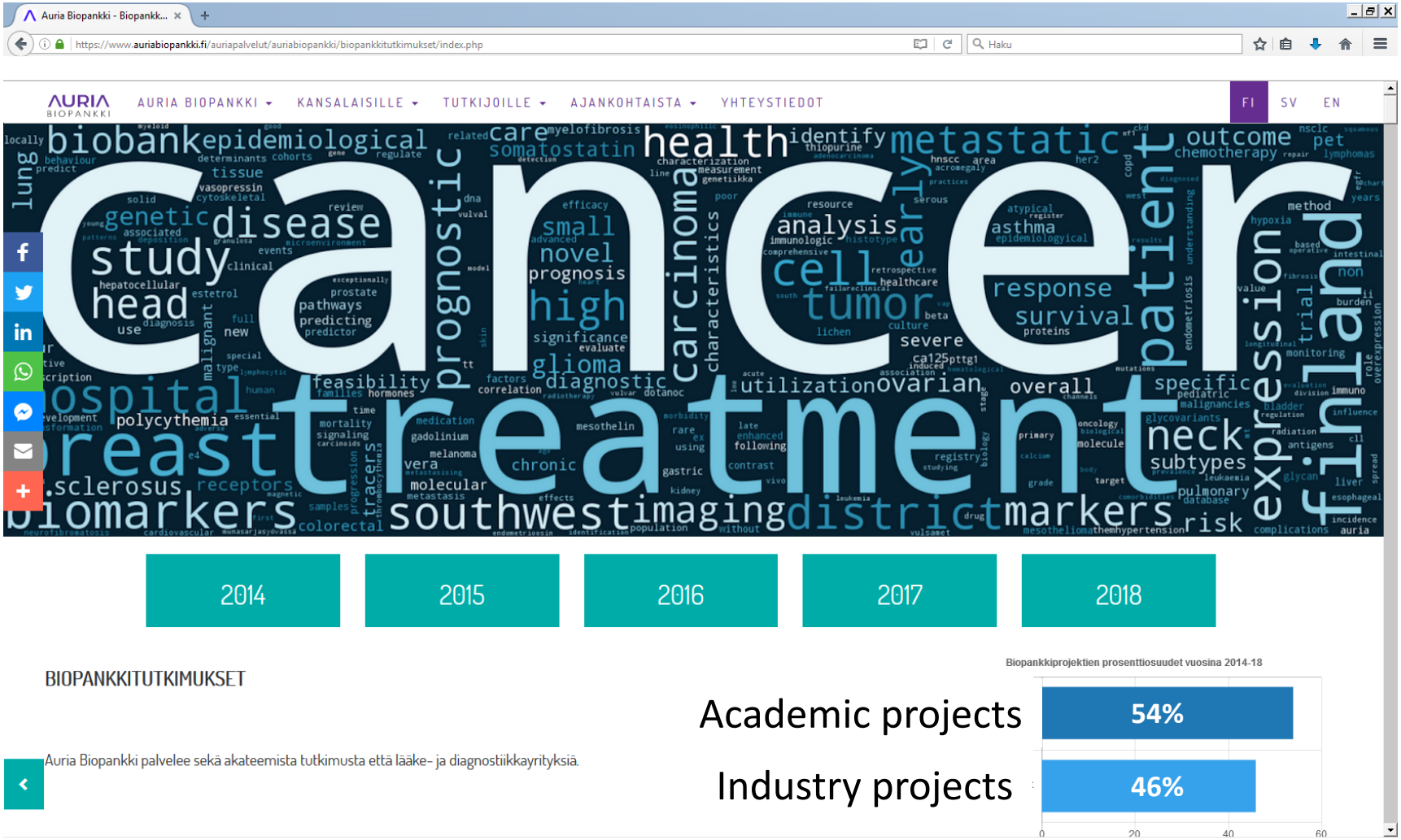
Who benefits?

- Researchers: Unique samples with large amounts of clinical data
- Industry: Research innovations, new forms of collaboration
- Healthcare: Data-driven healthcare, clinical decision support
- Patients: Better healthcare, personalized treatments

What is needed?

- Bio(data)banks and data lakes with big data
- Data scientists to turn data into knowledge
- Courage to work with the new methods
- Legal frameworks, research funding, public support

Information on biobank research projects



Biobanking in Finland

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