Genomic Medicine Sweden
Implementing precision medicine at the national level

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Precision medicine

To get the right diagnosis and to give the right treatment to the right patient
## European initiatives, 2013-2025

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>COMPANY/INSTITUTION</th>
<th>TIME</th>
<th>SCOPE</th>
<th>FUNDING</th>
<th>PROGRESS</th>
<th>MEDICAL FOCUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENGLAND</td>
<td>Genomics England Ltd. (GeL)</td>
<td>2013-2018</td>
<td>100,000 genomes</td>
<td>£411 M</td>
<td>50,000 genomes</td>
<td>Rare Diseases, Cancer</td>
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<tr>
<td>SCOTLAND</td>
<td>The Scottish Genomes Partnership (SGP)</td>
<td>2015-perpetual</td>
<td>~3,000 genomes</td>
<td>£23 M</td>
<td>~3,000 genomes</td>
<td>Rare Diseases, Cancer</td>
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<tr>
<td>THE NETHERLANDS</td>
<td>Hartwig Medical Foundation (HMF)</td>
<td>2015-2017</td>
<td>&gt;10,000 cancer patients</td>
<td>€30 M</td>
<td>~3,000 patients</td>
<td>Cancer</td>
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<td>FRANCE</td>
<td>France Médécine Genomique (AVIESAN)</td>
<td>2015-2025</td>
<td>235,000 WGS/annum by 2020</td>
<td>€670 M (-2020)</td>
<td>Two platforms selected</td>
<td>Rare Diseases, Cancer</td>
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<td>IRELAND</td>
<td>Genomics Medicine Ireland (GMI)</td>
<td>2016-perpetual</td>
<td>45,000 genomes</td>
<td>$40 M</td>
<td>Incorporated Series A</td>
<td>Population studies, Rare Diseases</td>
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<td>GREECE</td>
<td>Precision Medicine Programme</td>
<td>2018-2019</td>
<td></td>
<td>€5 M</td>
<td></td>
<td>Cancer</td>
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<tr>
<td>FINLAND</td>
<td>Finland’s Genome Strategy (FGS)</td>
<td>2017-2020</td>
<td>National infrastructure (operational by 2020)</td>
<td>€17 M (Request for €50 M)</td>
<td>Planning phase</td>
<td>Rare Diseases, Cancer, Pharmacogenetics, Genetic Risk Susceptibility</td>
</tr>
<tr>
<td>NORWAY</td>
<td>The Norwegian Strategy for Personalised Medicine in Healthcare</td>
<td>2017-2021</td>
<td>&lt;13,000 WGS/annum</td>
<td>NOK 8 M (pre-analysis)</td>
<td>Planning phase</td>
<td>Rare Diseases, Cancer, Infectious Diseases</td>
</tr>
<tr>
<td>DENMARK</td>
<td>National Strategy for Personalized Medicine (Per Med)</td>
<td>2017-2020, 2020-perpetual</td>
<td>DKK 5 M (pre-analysis)</td>
<td>DKK 100 M</td>
<td>Initiated</td>
<td>-</td>
</tr>
<tr>
<td>SWEDEN</td>
<td>Genomic Medicine Sweden</td>
<td>2017-2023</td>
<td>45,000 samples/year</td>
<td>SEK 4 M (pre-analysis)</td>
<td>Planning phase</td>
<td>Rare Diseases, Cancer, Complex Disease, Microbiome</td>
</tr>
</tbody>
</table>
What do we want to achieve with GMS?

To offer all patients in Sweden:

- The best available diagnostics – using next-generation sequencing technologies
- Precision medicine – the right treatment to the right patient

Through a national effort offer equal care independent of healthcare region

- Build a unique national resource
- Research and innovation
How do we create a leading PM infrastructure?

Building on existing national resources:

- Science for Life Laboratory (SciLifeLab)
- Biobank Sweden
- Swedish National Quality Registries
- Regional Cancer Centres
- Centres for Rare Diseases
- Clinical studies in Sweden (trial alliances)
**GMS focus areas**

**Rare Diseases:**
- Whole-genome sequencing
- >3,500 samples in routine diagnostics at Karolinska University Laboratory
- >35% more diagnoses

**Cancer:**
- Solid tumors and leukemia:
  - Gene panels
  - (RNA-sequencing)
  - (WGS)
- >5,000 samples/year in routine
GMS implementation strategy

- New national infrastructure in healthcare:
  - 5 national reference groups
  - 5 technical WP
  - 4 ELSI/education/pharmacogenetics WP

- **250-300** participants in the different groups

- Regional Genomics Medicine Centers (GMC)
Genomic Medicine Centers

- At the university hospital in collaboration with the university
- Build on regional expertise and investments
- Broad competence in advanced molecular diagnostics
- Build expert PM teams
- Node for inclusion in clinical trials
- Promote coordination at national level
Genomic analysis ➔ Variant list ➔ Clinical Diagnostics

- Known disease genes
- Multidisciplinary conferences
- New biomarkers
Clinical whole-genome sequencing

Delivery to SciLifeLab
Manual or Automated library preparations
Rapid sequencing

Automated, secure data processing and QC

Dedicated HPC cluster for data processing
Alignment, variant call, functional annotation
Sample specific quality measurement
Browser-based data presentation for collaborating physicians

Clinical interpretation and reporting

>1000 samples/years, Clinical Genetics, CMMS, Clinical Immunology & Clinical Genomics
Cancer sequencing – today

Mutations in lung cancer

Targeted therapy

Lung cancer

- Trastuzumab
- Panitumumab
- Gefitinib
- Osimertinib
- Imatinib
- Cetuximab
- Erlotinib
- Afatanib
- Crizotinib
- Vemurafenib

50% of Swedish patients tested with gene panel

- 1st generation gene panels (5-50 genes)
- 2nd generation gene panels (500 genes)
  All treatable targets, all forms of cancer
- 3rd generation - global sequencing
  WES, WGS, RNA-Seq
Hematology: increasing number of relevant genes....

Myeloid gene panel (54 genes)

Splicing Factors (~50%)
- SF3B1 (18%)
- U2AF1 (12%)
- SRSF2 (12%)
- ZRSR2 (5%)
- Others (5%)
Rarely co-occur with each other

Epigenetic Regulators (~45%)
- TET2 (20%)
- ASXL1 (15%)
- DNMT3A (12%)
- EZH2 (5%)
- IDH1/2 (5%)
- Others (5%)
Often co-occur except for TET2 and IDH

TP53 and no SF or ER (~5%)
Often complex karyotypes with frequent del(5q), abnormal chromosome 7, and monosomies

No Common Abnormality (~5%)
Karyotype Abnormality Only (~5%)

Mutations in Other Genes Only (~15%)
- Transcription Factors
  RUNX1, ETV6, PHF6, GATA2, ...
- Kinase Signalling
  NRAS, KRAS, JAK2, CBL, ...
- Cohesins
  STAG2, SMC3, RAD21, ...
- DNA Repair

Rafael Bejar, and David P. Steensma, Blood 2014;124:2793-2803

Lucia Cavelier, Uppsala
Myeloid gene panel (54 genes) – MDS

- Hemolysis, mild dysplasias, normal cytogenetics
NGS-based diagnostics in hematology

Panel diagnostics
- Capture panel (er)
  - Lymphoma incl CLL
  - AML MDS MPN

Fusionstranscripts and classification
- Transcriptome analysis
  - RNA seq
  - AML
  - ALL

WGS/WES
- Inherited hematology
  - In silico panels
- Digital karyotyping
  - Implementing WGS in acute leukemias

Diagnostics
- Prognostication
- Monitoring
GMS – Pediatric Cancer

- National collaborative effort:
  - Swedish Childhood Tumor Biobank
  - Pediatric hematology and oncology
  - GMS-hematology/solid tumors
  - Barncancerfonden

- WGS on 420 children per year
Time plan GMS

- **Formation**
- **Start-up**
- **Pilot studies**
- **Implementation and upscaling**
- **New areas**

- **2017**
  - Formation
  - Start-up

- **2018**
  - Pilot studies

- **2019**
  - Implementation and upscaling

- **2023**
  - Evaluation 1

- **2028**
  - Evaluation 2
  - Evaluation 3
  - Evaluation 4
Thank you for listening!