Molecular Pathology Practice in Europe: Sweden

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Swedish Molecular Pathology (MP) - outline

• Basic facts
• Future perspectives
• Structured to mirror the other presentations
• Summed up in handout
Who performs MP in Sweden?

• Typically a team made up of pathologists, molecular biologists and biomedical laboratory scientists

• Molecular characterization of hematological malignancies are often partly performed in other laboratory specialities like clinical genetics

• There is no legal authorization and no special qualification/diploma is required to perform MP
Swedish tests & testing strategies

• Treatment predictive testing in solid tumors largest volume (Breast – ERBB2; NSCLC – EGFR, ALK, ROS1 etc; CRC – RAS & RAF, MM – BRAF)

• Almost 10 000 NGS analyses and 15 000 “other” MP tests yearly

• Sequencing in gene panels – pricing roughly 1 000 euros

• Predicitive and diagnostic testing generally dependent on WHO recommendations and other consensus documents

• Malignant hematology, pediatric malignancies and bone-/soft tissue tumors most extensively characterized (up to WES + RNAseq)

• HPV screening set up within pathology in some regions
NSCLC in Sweden – alternate strategies

Common for all labs
• Morhphology + IHC for diagnosis
• PD-L1 IHC (might be centralized)
• DNA gene panel (centralized)

Differing strategies for fusion genes and Met exon skipping
• IHC+FISH (for ALK, ROS1 fusions)
• RNA panels (for fusions and skipping)
• Nanostring (for fusions and skipping)
Liquid biopsies

- In clinical routine only for NSCLC
- Mainly for detecting TKI resistance mutations
- Some analyses in a primary setting in which tissue/cytology is sufficient for diagnosis but not molecular characterization
- ddPCR and NGS main methodologies
Funding of MP in Sweden?

- MP paid for by the clinical department referring to testing
- Temporary regional funding for implementation
- No system for reimbursement
- A gene panel for treatment predictive purposes – 1 000 Euros
Involvement of pharma and dx companies?

- No current funding of tests from pharmaceutical companies
- Facilitation of training and education
- Testing through commercial external testing currently not recommended within the publicly funded health care
- Roche has applied for approval for FoundationOneCDx
- Broader discussion with authorities initiated
Swedish MP instrumentation and methodology

- Focus on NGS with a trend towards upscaling and collaboration
- QPCR, MLPA, pyrosequencing etc for specific purposes
- Sanger no longer used for somatic testing.
- Fully automated devices rarely used but has been introduced for MSI testing in smaller labs
Swedish Molecular Pathology Map

• 10 million inhabitants
• All covered by MP testing
• 21 regions are responsible for health care
• Nearly 30 pathology labs
• 7 nodes in a national precision medicine initiative
Swedish Molecular Pathology Map

• 7 nodes in a national precision medicine initiative

• 2 additional satellites performing NGS
Genomic Medicine Sweden – Time line

- **2017**: Formation
- **2018**: Pre-study
- **2019**: Bottom up initiative (SciLifeLab)
- **2021**: Top down – new national steering board (Vinnova June-Oct 2018)
- **2022**: Start-up
- **2023-2029**: Implementation (Vinnova Nov 2018 - Dec 2020)
- **2029**: Extension phase (5-10 year perspective)
Genomic Medicine Sweden - aims

- Cutting edge diagnostics – initial focus on next generation sequencing technologies
- Precision medicine – the right treatment to the right patient and the right time
- Through a nationwide collaborative effort offer all patients equal care regardless of healthcare region
- A unique national research database
- Innovation and industry cooperation
Genomic Medicine Sweden – central functions

- Harmonized informatics and cost effective data storage
- Pooled resources and coordinated efforts on assay development, validation and implementation
- Work packages to solve key issues
Genomic Medicine Centers

- Relies on the national infrastructure and supports national collaborative efforts
- Governed by the university hospitals and their corresponding medical faculties
- Represents the healthcare regions and supports highly specialized medical care
- Access to advanced molecular diagnostics and decision support
- Hub for inclusion in clinical trials
# Basic concepts - organisation

## National infrastructure

<table>
<thead>
<tr>
<th>National reference groups</th>
<th>Informatics</th>
<th>Ethical and legal aspects</th>
<th>Health economy</th>
<th>Education &amp; communication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rare Diseases</td>
<td>Data processing</td>
<td>Decision support</td>
<td>Data sharing</td>
<td>Data storage</td>
</tr>
<tr>
<td>Hematology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solid tumors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microbiology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complex diseases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacogenomics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Regional infrastructure

- GMC Uppsala
- GMC Norr
- GMC Örebro
- GMC Karolinska
- GMC Västra
- GMC Sydöstra
- GMC Syd
Genomic Medicine Sweden – Funding

Formation

Pre-study

Start-up

Implementation

Bottom up initiative

Swelife – Vinnova

8 million euro

Vinnova (- Dec 2020)

Extention phase – funding still lacking
Genomic Medicine Sweden – examples of current projects

• National gene panels for hematological malignancies ordered and solid tumors panels in late design stage
• WGS + RNAseq for all pediatric maligncies in collaboration with BTB (the national pediatric tumor biobank)
• WGS pilots in hematological malignancies and rare disease
• Pilots for a national computational and storage solution (raw and variant data with added meta data)
Accreditation

• ISO 15189 is the ISO standard used for MP (and histomorphological diagnostic work)

• Accreditation is not mandatory to perform diagnostic work

• There are sites that have specific assays accredited but none has an accreditation for the complete MP work flow

• Most sites plan to apply for a complete accreditation
Quality assessment & quality assurance

• National EQA schemes starting with KRAS in CRC (2008, 2008, 2009)
• Joined European efforts in 2009 (ESP, IQN-)
• Additional national schemes in select areas (e.g. BRAF in MM, HER2/ERBB2 in gastric cancer)
• Decision to rely on European EQA work
• Volumes and aggregated data on variants from all labs 2011-2015
• A variant database linked quality registries to couple variants with treatment outcome as part of Genomic Medicine Sweden’s
Analyses 2011-2015 (NSCLC, CRC, MM)
KRAS: Activating mutations 2011-2015 (%)

All activating mutations (%)

Individual mutations (%)

- p.Gly12Asp
- p.Gly12Val
- p.Gly13Asp
- p.Gly12Cys
- p.Gly12Ala
- p.Gly12Ser
- p.Gly12Arg
- Codon 61
- Codon 146
- Codon 137
- Codon 59
Training

• MP in curriculum for residents but no mandatory training for specialists
• Yearly national short course but no in-depth educational modules
• No structured add on for molecular biologists
Inclusion of MP results in pathology reports?

- Recommended nationally and an aim in all institutions
- Degree of integration varies between disease areas and health care regions
- Layout and content dependent on the needs and background of involved clinicians
- Harmonization ongoing
Conclusions - Sweden

• All MP testing needed for indicated diagnostics and treatment prediction performed

• Hope to upscale MP to general, comprehensive up front testing through the national Genomic Medicine Sweden effort but financing still unclear

• Training of pathologists (and other health care professionals) an important challenge