Histopathology to Molecular Pathology

Thomas Kerr
Principal Biomedical Scientist
Laboratory Genetics
QEUH
Oxford Dictionary
Definition of Change

The substitution of one thing for another.

“we need a change of government”
Embracing Change

Service Development and Service Improvement
Glasgow Royal Infirmary

Dr Anne Marie McNicol
Prof. Fred Lee
Maura Farquharson
Dr Bob Jackson
Dr Colin Stewart
John McCorriston
Neuropathology

Resistance to change to maintain specialisation to prevent merger with general pathology

Dr Willie Stewart

Prof Roy Rampling

1p19q and MGMT analysis
Glasgow Royal Infirmary

- Molecular pathology section within North Glasgow Pathology department
  - Lymphoma
  - HER2
  - Sarcoma
  - CNS tumours
  - Adult BMT and haemato-oncology testing

The Calman review of genetics in relation to healthcare in Scotland
Better health better care action plan
Better cancer care action plan
Clinical trials
SPAN & Scottish cancer group networked approach to HER2 FISH testing
A molecular pathology service should be developed and run as a NSD supported consortium, mirroring the Scottish genetics laboratory consortium for diagnosis of constitutional genetic abnormalities.

To ensure the stability of the services, equity of access and service development

Linked to the Scottish cancer taskforce, cancer networks and Scottish medicines consortium so that there is early coordinated planning for new testing.
Molecular Diagnostics 2013

- The molecular genetics, molecular pathology and molecular haematology have an expanding workload.
- The numbers of molecular tests is predicted to increase dramatically over the coming years.
- To cope with this increase, some of the laboratory workflow will be automated.
- The combined expertise of the scientists in all these laboratory areas will ensure the Glasgow service is fit for the future.
- We will be able to develop and deliver a better and more efficient diagnostic service to all our patients.
Automated DNA and RNA Extraction
Automated Workflow
Laboratory Genetics

• Constant state of flux
• Introduction of new services including lung cancer, colon cancer, melanoma, digital PCR and NGS
• Integration of services and streamlining of work flows
• New assays for lymphoma, CNS tumours and ovarian cancer
• Automation
• Training in new testing platforms, new assays to work in a department that I was not trained to work in as a state registered BMS
Laboratory Genetics

• Constant interaction with user groups especially pathology, haematology and clinical genetics

• Scientist led discipline unlike pathology which is led by consultant pathologists

• Member of the genetics management group that is tasked with developing and delivering this service

• Our responsibility if we fail to deliver
Sakura automated microtome
## Mutation Testing

Next Generation Sequencing

<table>
<thead>
<tr>
<th>TruSight Myeloid Sequencing Panel Gene List</th>
</tr>
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<tbody>
<tr>
<td>ABL1</td>
</tr>
<tr>
<td>ASXL1</td>
</tr>
<tr>
<td>ATRX</td>
</tr>
<tr>
<td>BCOR</td>
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<tr>
<td>BCORL1</td>
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<tr>
<td>BRAF</td>
</tr>
<tr>
<td>CALR</td>
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<td>CBL</td>
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<tr>
<td>CBLB</td>
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<tr>
<td>CBLC</td>
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<tr>
<td>CDKN2A</td>
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Next Generation Sequencing
**Patient 1: 51 year old Male**

Differential diagnosis here lies between myelodysplasia or chronic myelomonocytic leukaemia

FLT3 ITD/NPM1 NOT Detected.

ELN risk classification: intermediate

<table>
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<tr>
<th>Gene</th>
<th>Variant</th>
<th>Notes</th>
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</table>
| RUNX1 | c.777dupT  
p.(Asn260*) | CR rate significantly lower, resistant disease rate higher and DFS, EFS, and OS, shorter for patients with a RUNX1 mutation compared with patients with wild type RUNX1. |
| EZH2 | c.1534C>T  
p.(Gln512*) | EZH2 is a prognostic biomarker, associated with overall shorter survival. |
| STAG2 | c.3085C>T  
p.(Gln1029*) | STAG2 often seen in high-risk MDS, high risk MPN as well as secondary AML. |
| ASXL1 | c.1926_1927insG  
p.(Gly646Trpfs*12) | Chromatin modifier – epigenetic regulator. This variant accounts for more than 50% of ASXL1 reported variants. Generally poor prognostic indicator. |
| SRSF2 | c.284C>T  
p.(Pro95Leu) | Poor prognostic indicator in MDS patients. |

Poor prognosis
**Gene** | **Variant** | **Notes**
--- | --- | ---
IDH2 | c.419G>A  
p.(Arg140Gln) | Possible drug target.  
Impact for prognosis is in patients <60 years.  
ASXL1 | c.1931_1956del  
p.(Gly648Hisfs*3) | Generally poor prognostic indicator.  
SRSF2 | c.284C>A  
p.(Pro95His) | Poor prognostic indicator in MDS patients.
What about the future?

molecular diagnostics

integration

combined genetics laboratory

cytogenetics