

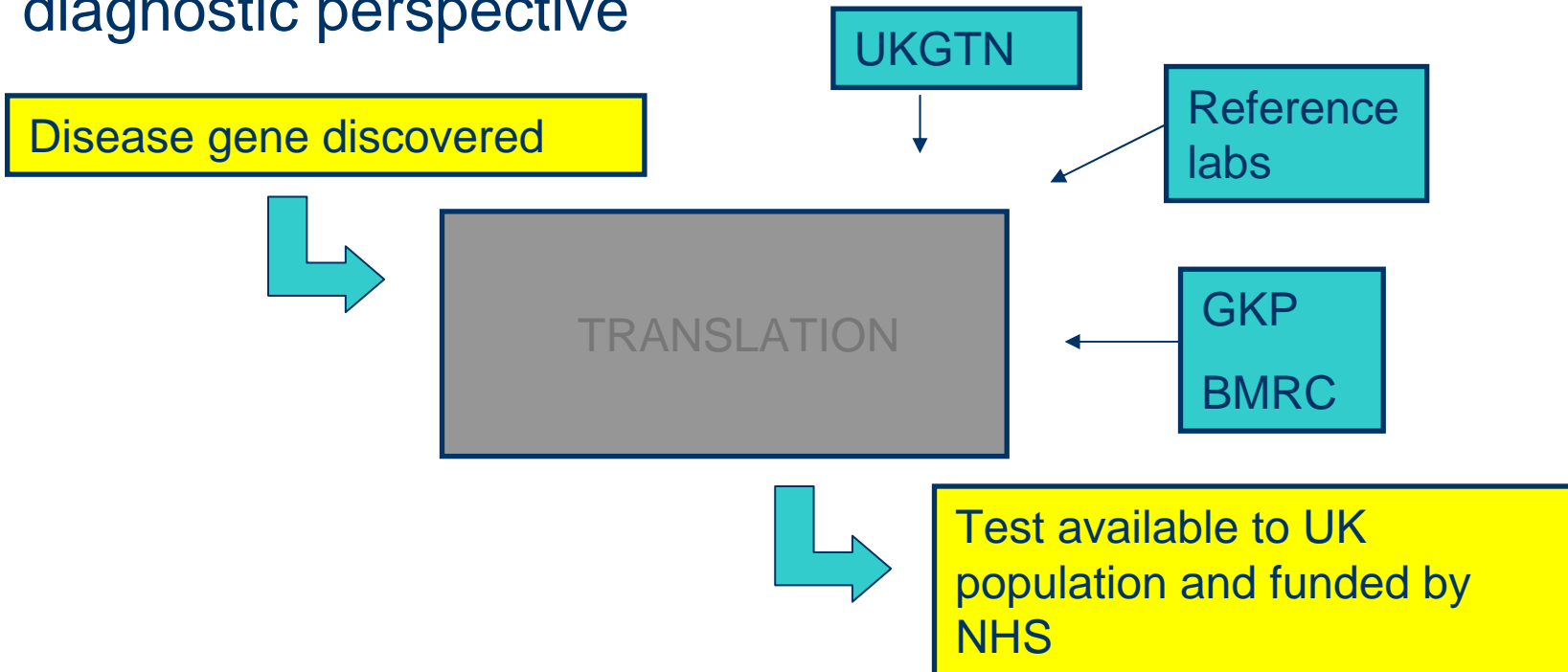
Translation from Research into Clinical Practise: diagnostic laboratory perspective

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UKGTN Scientific Adviser

Aims (1)

- Describe the translational process from the diagnostic perspective



Aims (2)

- To consider an extended role for UKGTN in commissioning of genetic testing in the future

Genetic Test Definition

- UKGTN
 - “tests for single gene germline disorders where nucleic acid is the analyte”

For example

Cystic fibrosis: CFTR

Familial Breast Cancer: BrCa1 and BrCa2

UK Genetic Services Network

22 Regional Genetic Services

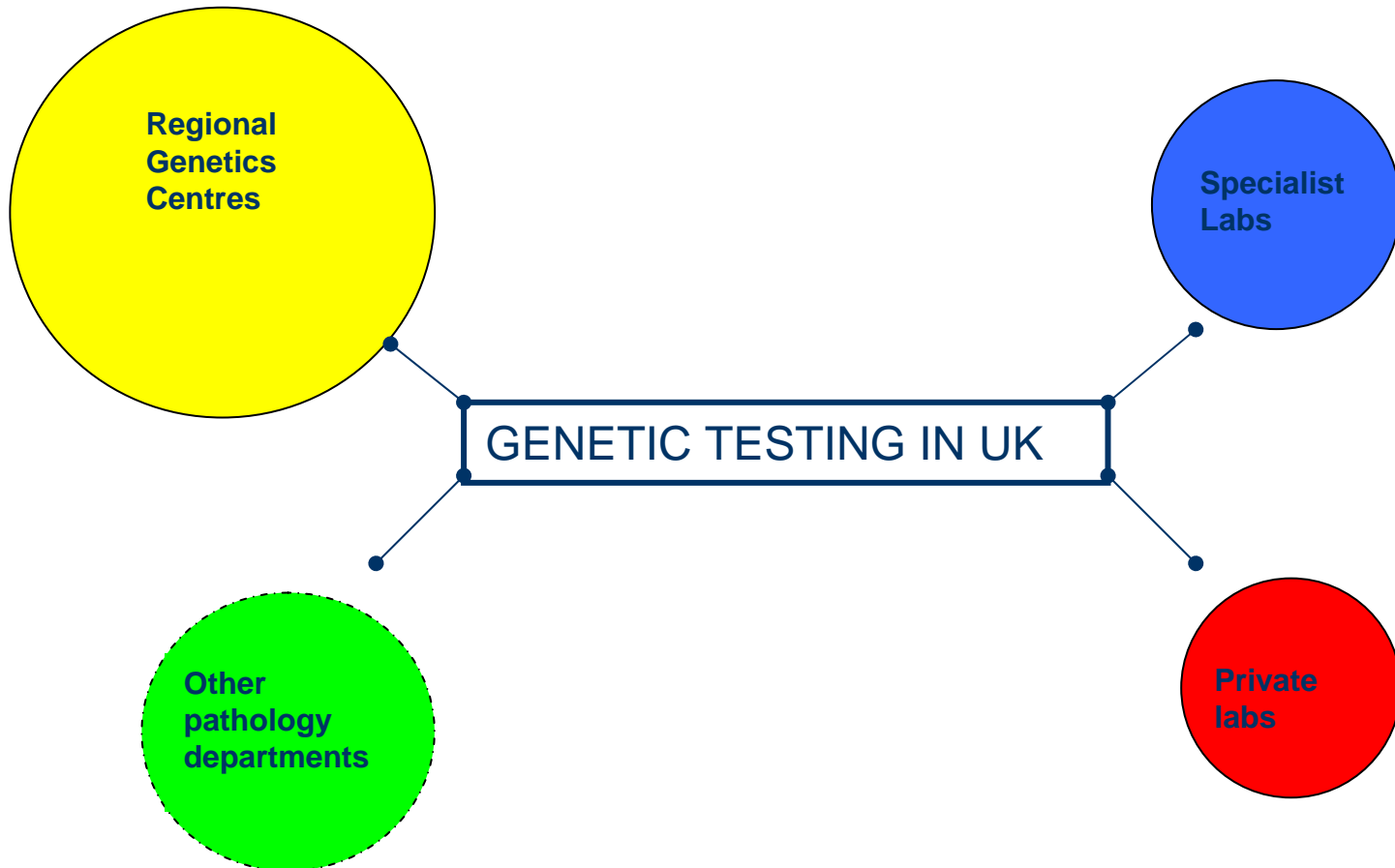
- 8 Molecular Genetic clusters.
- Cytogenetics
- Clinical Diagnosis
- Counselling
- Research

Two National Genetics Reference Laboratories

UK Genetic Testing Network
Genetic Knowledge Parks
National Genetics Education and Development Centre



Genetic testing in the UK



UK Genetic Testing Network

- Formalised in 2003, funded by the DH
- Promote equity of access to genetic tests in the UK
- Remit is limited to single gene, germline disorders where nucleic acid is the analyte
- Online Directory and Database of member laboratories and the service levels provided for each disease/gene
 - www.ukgtn.nhs.uk

UKGTN structure and working arrangements

P R O J E C T T E A M	UKGTN WORKING GROUPS	S T E E R I N G G R O U P
	Laboratory scientists Clinicians Commissioners Patient representatives Academics	
	Lab membership and audit Gene Dossier and directory Service development Commissioning Systems and communication	

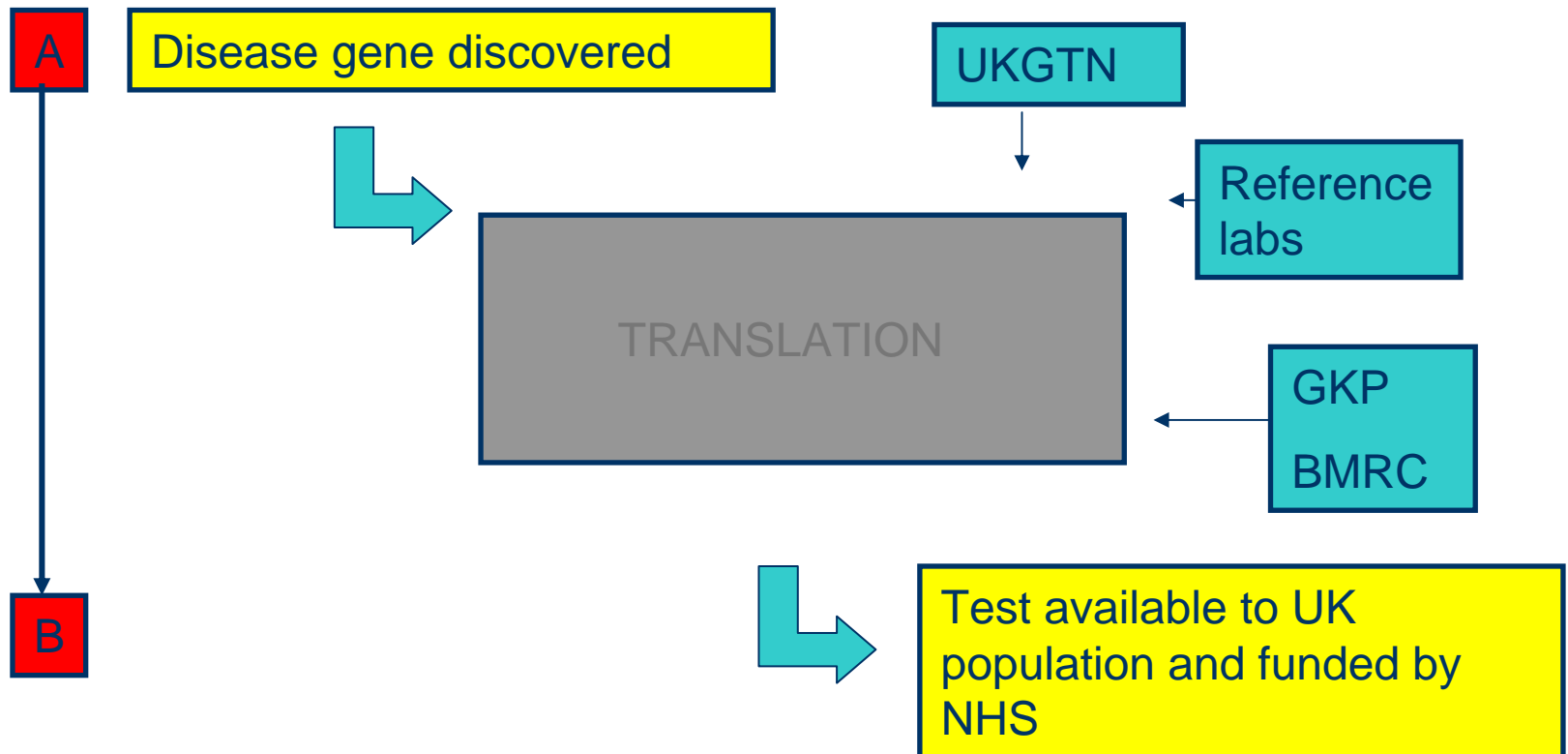
UKGTN Membership

- 1st wave:
 - all regional molecular genetics laboratories
 - specialist molecular genetics laboratories
- 2nd wave:
 - technical providers but only in partnership with a RGC
- 3rd wave:
 - cytogenetics laboratories

National Genetics Reference Laboratories

- Manchester and Salisbury
- Support the Network
 - Informatic tools and systems for diagnostics
 - Technology Assessment
 - Quality Assurance

Translational Process



Translation

- The work required to provide proof of
 - Analytical validity A
 - Clinical validity C
 - Clinical utility C
 - Ethical, legal and social implications E
- for a disease in a given target population
- Defined and formalised by UKGTN into the
GENE DOSSIER

Translation to Commissioning

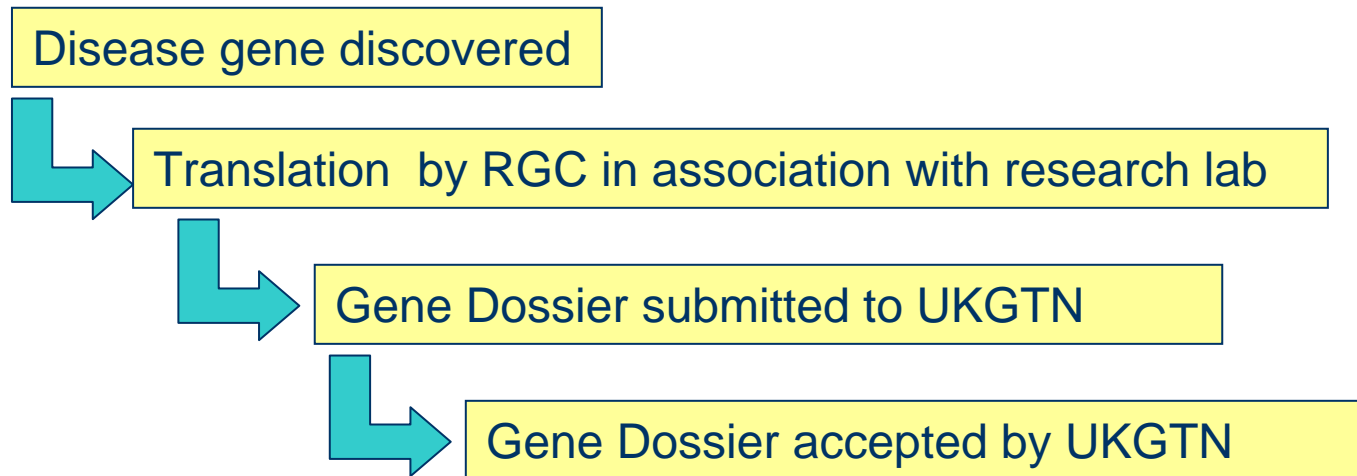
Disease gene discovered



Translation by RGC in association with research lab

- **Clinical scientists in RGC's as job role**
 - **Funded by host Trusts**
- **Research / NHS partnerships**
 - **Eg Genetics Knowledge Parks (pre 2007)**
 - **Sudden cardiac death (Oxford)**
- **Reference Labs / Research**
 - **Autosomal Dominant Retinitis Pigmentosa (Manchester)**
- **Biomedical Research Centres (2006)**
 - **Autosomal Recessive Retinitis Pigmentosa (Oxford)**

Translation to Commissioning



Gene Dossier

- Details and prevalence of the condition
- Target population
- Complexity of the test
- Clinical context in which the test is to be used
- Analytical validity
- Clinical validity and utility
- Cost
- Referral pathway and referral criteria

Gene dossier: Long QT syndrome

Disease – name and description	Long QT Syndrome (Romano-Ward)
OMIM number for disease	LongQT Syndrome (Romano-Ward) includes:- LQT1=192500 LQT2=152427 LQT3=603830 LQT5=176261 LQT6=603796
Gene – name and description (please provide any alternative names you wish listed)	<p>LQT1 KCNQ1 (KVLQT1) The alpha subunit of the slowly activating potassium delayed rectifier I_{ks}.</p> <p>LQT2 KCNH2(HERG) The alpha subunit forming the rapidly activating potassium delayed rectifier I_{kr}.</p> <p>LQT3 SCN5A The alpha subunit forming the cardiac sodium channel.</p> <p>LQT5 KCNE1 (mink) The beta subunit of the slowly activating potassium delayed rectifier I_{ks}.</p> <p>LQT6 KCNE2(MiRP1) The beta subunit forming the rapidly activating potassium delayed rectifier I_{kr}.</p>

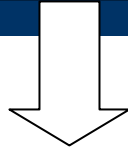
Referral Pathway Template – .

Population A

Individuals with a clinical diagnosis or probable clinical diagnosis of LongQT syndrome.

Population B

At risk relatives in families where a pathogenic mutation has been identified in the proband.



Population A

Referrals accepted from:

Clinical Genetics Departments

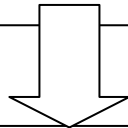
Consultant Adult and Paediatric Cardiologists in liaison with their local Clinical Genetics Department

Coroners and Pathologists

Population B

Referrals accepted from:

-Clinical Genetics Departments



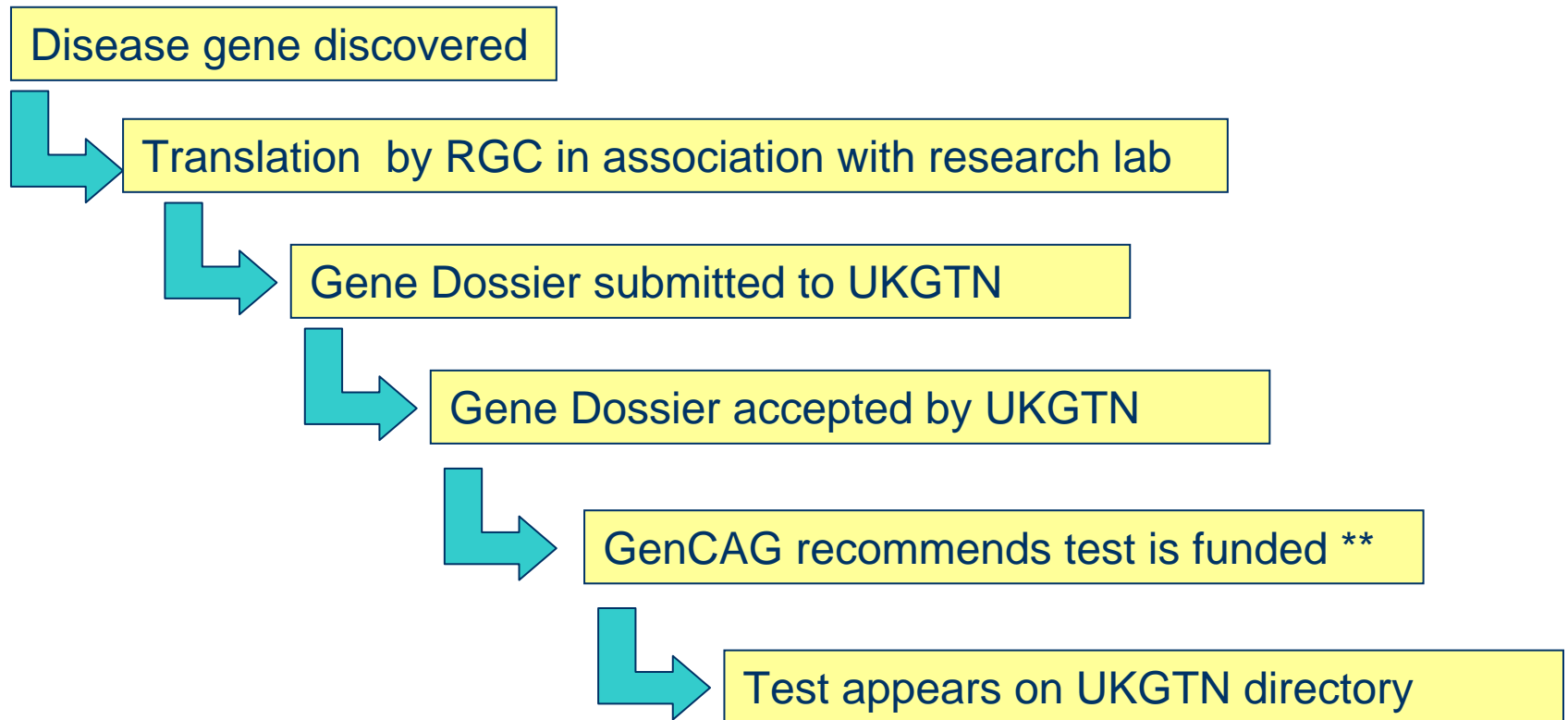
-Minimal referral criteria will be set.

-Referrals will be assessed by the SCD Team

(Clinical scientist in charge of disease, Consultant Clinical Geneticist [Dr E. Blair], Cardiovascular Genetic Counsellor and Consultant Cardiologist [Professor H. Watkins])

300 Gene Screen
300 Single mutation tests
(Presymptomatic and Diagnostic)

Translation to Commissioning



Translation cont

GenCAG ***recommends*** test is funded



GenCAG ***advices*** Commisisoners to fund tests for local population and informs of cost of test for population



LSCG's decide whether to fund test for local population and increase budgets of RGC's

Gene dossier: rejections

Common problems:

- May have limited clinical utility
- May still really be in the research phase
- May have poor sensitivity and specificity
- Referral pathway and testing criteria may not be thought out

Issues and problems for laboratories

- UKGTN is **not** a statutory regulatory body, it is a network of laboratories and has an advisory role to the DH:
 - *Lever for change*
- It is often not possible to undertake rigorous test evaluation especially for sensitivity and specificity
- Translation and UKGTN process may be successful but may not be supported by local commissioners
 - *Equity of access*

Issues and problems

- Trusts may not support business cases for staff and equipment especially for referrals outwith catchment area
- UKGTN does not limit or designate the number of providers
 - *Planning and service delivery*

The future role for UKGTN in test evaluation

- Currently addresses inherited or heritable disorders where DNA is the analyte
- Should it broaden it's scope to more complex disorders?
- Should it confine itself to DNA as the analyte?

Future Role of UKGTN

