Implementation of arrayCGH into NHS genetics services

The Patient's Perspective

Beverly Searle PhD
Chief Executive Officer

Unique -
The Rare Chromosome Disorder Support Group

For whom is a diagnosis sought?

- Individuals with an abnormal phenotype but no diagnosis and who have had no testing
- Individuals with an abnormal phenotype but no diagnosis following more conventional analysis such as karyotyping, FISH, MLPA
- Individuals with an abnormal karyotype seeking a more precisely defined diagnosis
- Couples seeking pre-natal diagnosis
- Couples who have experienced multiple miscarriages, fertility problems, stillbirths or the birth of a child with a chromosomal imbalance

Why do families seek a diagnosis?

- Explanation and a name for their child's symptoms
- Information about and knowledge of their child's disorder
- Prognosis and possible understanding of the child's future needs
- Improved care management pathways and clinical support
- Timely treatments and therapeutic interventions
- Surveillance of and vigilance for the onset of associated medical conditions
- Curtailment of the endless round of numerous, costly (to the families and to the NHS) and often distressing and unnecessary interventions and appointments over many years
- Improved reproductive options and the ability to plan for future pregnancies
- Precise advice on risk to other family members

Why do families seek a diagnosis?

- “Just to know”
- Closure
- “Not a neurotic parent” - Validation of their concerns about their child
- Finding an appropriate support group
- “Not the only one” - Alleviation of isolation
- Finding others with a similar disorder and experiences
- Possibly improved access to other special needs services

Perceived Advantages of arrayCGH

- Ability to detect minute imbalances across the genome undetectable by more conventional methods like karyotyping, FISH or MLPA
- Ability to detect sub-microscopic imbalances at or near the breakpoints in affected individuals with de novo apparently balanced translocations
- Enables diagnosis of more previously unrecognised syndromes than is the case with conventional methods
- One test might avoid an endless round of other distressing tests
- Greater precision over genes that are or are not deleted or amplified, leading to introduction of appropriate screening and preventive treatments or reassurance and avoidance of unnecessary screening or preventive treatments
- Potentially more precise knowledge of the likely outcome for the child and the care management pathway to adopt
- Far more precise and meaningful lab reports than with conventional karyotyping
- Emergence of web-based syndrome-specific support groups for families with microdeletion/duplication syndromes under Unique umbrella extends social and emotional support to families

Perceived concerns over arrayCGH

- ArrayCGH will not detect truly balanced translocations or mosaicism
- Will access to existing methodologies like karyotyping be maintained for some families?
- Of major concern is that new genomic variants are frequently of uncertain significance
- How will results be interpreted in clinical practice? There are still gaps in understanding gene function and interaction
- Families with polymorphic structural variants sometimes have the mistaken impression they have a genetic defect
- Varying nomenclature can be even more difficult to understand than with karyotypes and can thus make aberrations more difficult for the lay person to compare between individuals but families welcome ISCN 2009's clear guidelines on nomenclature
- Permission has not always been sought before carrying out arrayCGH and timely, appropriate genetic counselling has not always been readily available or offered
- Accurate and timely genetic counselling is critical, especially if arrayCGH were to be used in PND

What families want

- In principle, arrayCGH at an appropriate level of resolution should be rolled out as the first line method of analysis post-natally with appropriate levels of funding made available to ensure this is a first class, equitable service, easily accessible to families UK-wide
- Testing must be accompanied by access to timely genetic counselling of the highest quality
- More conventional types of analysis need still to be available so balanced translocations and mosaicisms are not missed
- ArrayCGH should be introduced as the first line method of pre-natal analysis ONLY when a high level of reliance can be placed on interpretation of the results
- Individuals with an existing karyotype should have the opportunity to access arrayCGH analysis to further refine knowledge and understanding of their aberration
- Standardised, easy to understand nomenclature (e.g. standardised bp coordinates) describing the aberration should be used and should relate back to chromosomal locus
- International databases of quality documenting phenotype-genotype correlations or normal polymorphic variants must be supported and consulted to provide the most up to date knowledge
- Genetic counsellors must ensure that families truly understand the limitations of arrayCGH analysis
- Suitable educational and information resources must be available for use by patients and their families

Take home message from families

- Appropriate levels of funding are critical to ensure arrayCGH is rolled out in an appropriate way (taking into account the concerns raised) and to the highest standards across the UK for the benefit of patients and their families

- It's vital that roll-out of arrayCGH is matched by stimuli for research, database collection of cases (e.g.Decipher), publication and ongoing education of genetics and other health professionals.

For more information please contact Unique

Website	**www.rarechromo.org**
Email	**info@rarechromo.org**
Telephone helpline	**01883 330766**
Write to us at	**P.O. Box 2189** **Caterham** **Surrey** **CR3 5GN** **UK**