GeNeXpreSS

Exome sequencing reaches the clinic

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Exome sequencing as a diagnostic test in the clinic[1,2]

Since its first use nearly five years ago, next generation sequencing has made significant inroads into research as well as diagnostic laboratories. Now here comes the proof for applying whole exome sequencing in the clinic for the diagnosis of genetic disorders.[1,2] Studies have shown that the diagnostic yield of exome sequencing is likely to be around 25%. Compared with other traditional diagnostic tests, this yield is of immense value for physicians. The cost of the test having come down significantly in the last two years, this is proving to be an important tool in the hands of clinicians. If give it to an expert clinician along with a well-defined phenotype, the success is bound to be far higher.

Another attempt to treat Duchenne muscular dystrophy[3]

Duchenne muscular dystrophy is a common genetic disorder and still lacks a specific curative therapy. Several efforts in the past have failed and ongoing trials are yet to yield a tangible result that can be translated to clinical practice. Wein and colleagues have demonstrated a truncated isoform generated by exon skipping that protects muscle from contraction-induced injury and corrects muscle force to the same level as that observed in control mice.[3] To begin with, they have demonstrated that this particular isoform results from usage of an internal ribosome entry site (IRES) within exon 5 in muscle from individuals with minimal symptoms despite the presence of truncating mutations. There's a long way to go, but several such efforts are probably necessary before we have a permanent solution, that continues to elude both clinicians and families.

Consanguinity affects the fetal outcome[4]

We all know consanguinity increases the incidence of birth defects, but how does it affect the fetal outcome? A study by Becker and colleagues has thrown light on this important aspect that we all face in our clinics routinely.[4] After adjusting for several factors, the incidence of congenital anomalies was found to be 2% for non-consanguineous couples versus 5.9% for consanguineous couples (6.1% in first cousin progeny and 1.9% beyond first cousin) i.e. an excess of 3.9%. The authors have concluded that prevalence of major fetal anomalies associated with consanguinity is higher than in evaluations based only on postnatal life, a message to take home for all those who marry a relative!

Genetic basis for febrile seizures[5,6]

We knew it, right? Many children with febrile seizures including MMR vaccine related febrile seizures have similar history in a sib or a parent. Some preempt the attack by medications when MMR vaccine is given. Two papers now provide the basis for these observations. Schubert and colleagues have shown that mutations in the *STX1B* gene explain autosomal dominant fever associated epilepsy whereas Feenstra and colleagues have identified common genetic variants associated with general and MMR vaccine–related febrile seizures.[5,6]

Susceptibility to enteric fever[7]

Susceptibility to infections is multifactorial and extremely rarely Mendelian. Dunstan and colleagues have identified HLA-DRB1 as a genetic locus that has a role in susceptibility to enteric fever.[7] Their

study conducted in subjects from Vietnam and Nepal, though lacking matched controls, implicates HLA-DRB1 as a major contributor to resistance against enteric fever, presumably through antigen presentation.

References

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