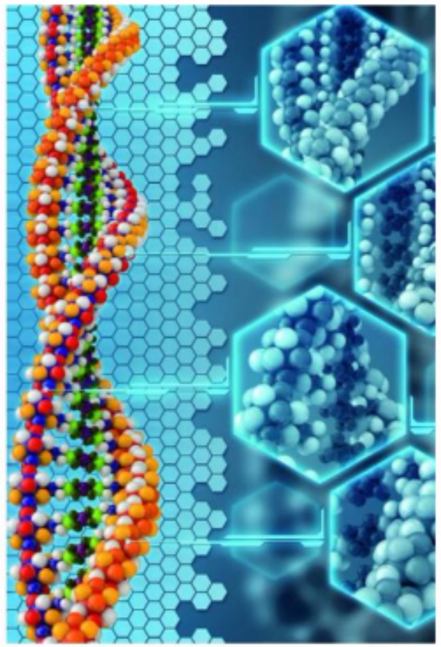
INSIGHT

# Inheritance patterns

**DR V L RAMPRASAD**
COO,
MedGenome

**Dr V L Ramprasad, COO, MedGenome,** gives an insight on ways to improve global health by decoding the information contained in an individual's genome



**A FAMILY'S** health history if recorded correctly through the years helps to understand how traits are passed on to their future generations. This set the pace for understanding the way familial characteristics are passed on from one generation to another is based on the patterns of inheritance discovered by an Austrian scientist and monk, Gregor Mendel. He is known as the father of modern genetics researched and discovered the essential patterns of inheritance during conducting experiments in the garden of the monastery he lived in. Mendel's studies of inheritance patterns in pea plants are a solid foundation for our current understanding of single-gene diseases in humans. Inheritance patterns describe how a disease is transmitted in families.

Through his research, Mendel inferred that human genes are present in pairs, one of each pair inherited from each parent. Some genes undergo changes which don't impact their functioning but the changes known as mutations do influence the functioning of the genes and may lead to disease. Such diseases are also called as Mendelian or monogenic diseases and they sometimes run in families. In the case of some families, members whose genes may experience a similar mutation don't necessarily have to experience the same symptoms (recessive). However, in the case of some other families, members whose genes experience dissimilar mutations may inherit the same traits/disease (dominant). Pedigree analyses of large families with many affected individuals can be used to determine whether a disease-associated gene is located on an autosome or on a sex chromosome, and whether the related disease phenotype is dominant or recessive.

### Different patterns of Inheritance

Diseases caused by mutations in a single gene are usually inherited through a simple process. This is dependent on the gene's location and the understanding of whether one or two normal copies of the gene are necessary. Though majority of the single gene disorders are uncommon, they affect millions of people in the US.

If a disease is caused by a mutated gene located on the X chromosome, it could be inherited in a dominant or a recessive manner. Single-gene disorders can be inherited via numerous methods like autosomal dominant, autosomal recessive, X-linked dominant and X-linked recessive though this does not apply to all cases.

### Autosomal dominant (mutation)

If a person has one copy of dominant mutation in each cell, the person gets affected by the disorder. At times, a person inherits mutant gene from her/his parent who is affected, e.g. Huntington's disease (a progressive neuro-degenerative disorder) caused by mutant huntingtin gene (HTT), then the person who inherits that mutant gene will develop the same disease. In this case, the presence of a single non-mutant or "wild-type" copy of the gene is not enough to prevent the disease. Individuals can inherit the mutant copy of the disease-associated gene from either an affected mother or an affected father. This type of inherited disease occurs in every generation of a family but can also develop in individuals who have no family history of the same.

### Autosomal recessive (mutation)

In the case of recessive genetic diseases, not every generation of a family gets affected. Because, autosomal recessive single-gene diseases occur only in individuals with two mutant alleles of the disease-associated gene. Remember, for any given gene, a person inherits one allele from his or her mother and one allele from his or her father. Therefore, individuals with an autosomal recessive single-gene disease inherit one mutant allele of the disease-associated gene from each of their parents. If both the parents have this type of a mutated gene, their children will definitely inherit the same. Thus, In pedigrees of families with multiple affected generations, autosomal recessive single-gene diseases often show a clear pattern in which the disease 'skips' one or more generations. Example, Phenylketonuria (PKU) associated with mutations in the gene that encodes the enzyme phenylalanine hydroxylase (PAH). Several other human diseases, including cystic fibrosis, sickle-cell anemia, and oculocutaneous albinism, also exhibit an autosomal recessive inheritance pattern.

### X chromosome-linked recessive:

Females carry two X chromosomes while males carry one X and one Y chromosome. This results in women carrying two copies of each X-linked gene but none of the Y-linked genes. Men carry only one copy each of X-linked and Y-linked genes Therefore, females with an X chromosome-linked recessive disease inherit one copy of the mutant gene from an affected father and the second copy of the mutant gene from their mother, who is most often a carrier (heterozygous, having one copy of non-mutant allele) but who might be affected (homozygous, having two copies mutant allele). Males, on the other hand, have only one copy of the X chromosome, which they always receive from their mother. Therefore, males with an X chromosome-linked disease always receive the mutant copy of the gene from their mother. Moreover, because men don't have a second copy of the X chromosome to potentially "cancel out" the negative effects of X-linked mutations, they are far more likely than women to be affected by X chromosome-linked recessive diseases. Hence, single-gene diseases that involve genes found on these sex chromosomes have somewhat different inheritance patterns than those that involve genes found on a person's autosomes (non-sex chromosomes, chromosome 1 to 22). The blood-clotting disorder hemophilia A is one of several single-gene diseases that exhibit an X chromosome-linked recessive pattern of inheritance, in which males having mutant copy of the factor VIII gene (F8) will always have haemophilia.

### X chromosome-linked dominant:

Families with an X chromosome-linked dominant disorder affect both males and females in every generation. In the case of X-linked inheritance, fathers pass the X chromosome to their daughters and Y chromosomes to their sons but mothers pass X-linked genes to both, their sons and daughters. Thus, females with an X chromosome-linked dominant disease can inherit the mutant gene from either an affected mother or an affected father, whereas males always inherit such diseases from an affected mother. Very few X chromosome-linked dominant diseases exist. For example dominant mutations in the phosphate-regulating endopeptidase gene (PHEX), which resides on the X chromosome, are associated with X-linked dominant hypophosphatemic rickets.

### Mitochondrial Inheritance:

The mitochondrion is an organelle that has its own DNA, often called as mitochondrial DNA (mtDNA). Mitochondria play essential roles in energy production and in various cellular processes such as metabolism and signal transduction. In humans, and most animals, although the sperm-derived paternal mitochondria enter the oocyte cytoplasm after fertilisation, their mtDNA is never transmitted to the offspring. Thus, this pattern of mtDNA inheritance is well known as 'maternal inheritance.'

> Families with an X chromosome-linked dominant disorder affect both males and females in every generation

Why are some genetic conditions more common in particular ethnic groups?

People living in geographical territories inhabited by their forefathers are prone to develop genetic orders carried by their ancestors. If any of the genes passed on includes a mutation that causes disease, a distinct genetic disorder will be visible in such individuals. Sachs disease and sickle cell anemia are widespread amongst the ethnic groups of Africa, European and the Mediterranean regions.

*References*
*https://www.ncbi.nlm.nih.gov/books/NBK115561*
*https://ghr.nlm.nih.gov/primer/inheritance/inheritancepatterns*
*http://www.enotes.com/homework-help/what-role-dna-storage-expression-transmission-702571*
*http://www.preservearticles.com/201203272896/what-is-the-importance-of-human-genome-project.html*
*https://ghr.nlm.nih.gov/primer/hgp/description*
*http://www2.le.ac.uk/departments/genetics/cgec/schoolscolleges/topics/inheritancepatterns*

INTERVIEW

# Attrition rates are very high in PPP models

In a conversation with **Raelene Kambli, Sabu Jose**, GM - Government, OEM & Corporate Accounts - India Cluster, Carestream Health, explains the challenges related to effective management of PPPs in healthcare

**How are public private partnerships designed in healthcare?**
PPPs in healthcare are mostly designed in a way where the government's role is such that it is involved in developing, financing and providing health infrastructure and services. Whereas the private sector player provides medical equipment or operates the healthcare facility.

**Given the backdrop that PPPs in healthcare don't seem to be very successful. What is your view on the same?**
When we thought of PPPs last year, we realised that many companies are withdrawing from these models of partnership with the government. States such as Gujarat, Madhya Pradesh are some states that withdrew from this model. And that is when we decided to go very slow in terms of partnering with the government. We also identified the reason behind the failure of such models. It is not just the money involved but it is about the operations and especially managing the manpower deployed on such projects.

**Do you think it is a lack of competency that is causing this problem?**
It is not only about competencies. They find it very difficult to retain people. One of my associate shared his experience working in a PPP and said that his team found extremely difficult to find people who would work dedicated in these project. The attrition rates are very high in such models. Moreover, most of these PPPs are done with equipment players and these players are not good with talent enrollment and do not have those strategies to retain people.

**So, what approach would you take in this regard?**
In my view, we need to split the component wherein the labour management should be dealt by the government.

> We have partnered with Kerala, Telangana, Maharashtra and Gujarat

**But do you think that the government is equipped to hire and manage specialised technicians especially the ones who operate high-end radiology imaging system?**
When a technician is hired by the government there is more responsibility involved. Employees understand that they cannot just quit and that they are been monitored as well. When hired by a private player they do not show that commitment.

**Apart from this, what is your opinion on rising import duty for medical equipment?**
Last year, the government introduced eight per cent tax on import duty and at the same-time they asked us to cut down on our price. If taxes are high, how will we be able to cut down on cost.

**Which are the states that you have partnered so far?**
We have partnered with Kerala, Telangana, Maharashtra and Gujarat.

**And which state according to you offers a better business environment?**
Telangana offers a better business environment. Apart from this, Kerala also offers a good business environment for us.

**What is different in these states?**
These states are different in their style of working as they always adapt what is new.

**Do you think there should a governing body that will look after PPPs and liaison between the government and the private sector?**
There are bodies such as HLL who are doing well but yes there should some sort of understanding between the two parties to make PPPs work.

*raelene.kambli@expressindia.com*