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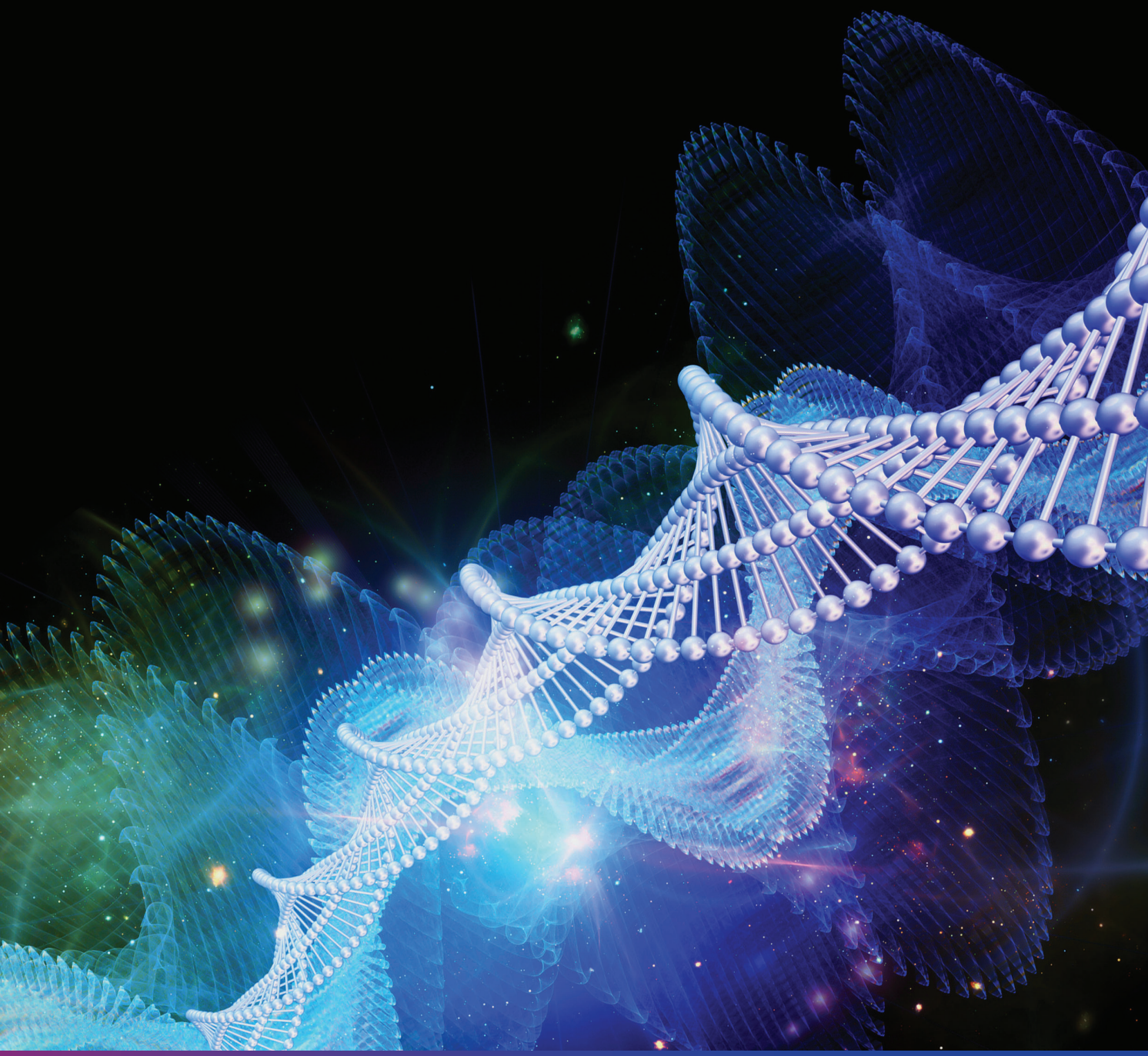
Internal Quarterly Newsletter



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Sanjay Kumar Sharma

Chief Commercial Officer

Management Speaks

Abnormalities due to genetic and congenital factors in India is the second most common cause of infant and childhood mortality. Recent observations from WHO states that "the hereditary genetic diseases are becoming a significant health burden in India". Factors contributing to this high prevalence include consanguineous marriages, high birth rate, absence of good diagnostic facilities, and a lack of expertise in genetic counselling. The demand & supply imbalance for clinical genetic testing in Indian context remained unaddressed till the early years in this decade.

Back in 2014, I met Sam Santhosh to discuss the scope of expanding clinical genetic testing service in India. Considering that there was a highly skewed scenario of demand vs. supply, and an enormous scope for business scaling, I enthusiastically took up this challenging assignment. Since then, there is no looking back!

Today, MedGenome boasts of its pinnacle position in Clinical Genetics Market in India and South East Asia. The relentless drive has helped MedGenome gain access in over 150 towns including Metros, Capitals, and Tier 2 & 3 towns. Have a pool of 6000+ prescribers spread over 600+ hospitals in Government, Private and Corporate settings. In addition, many of the service providers are outsourcing services to MedGenome as their trusted B2B partner. So far, over a lac of exome sequencing tests are being prescribed by renowned clinicians across the length & breadth of India. Since inception, MedGenome's clinical genetic testing offerings has considerably contributed in genetic burden abridgement in India.

The journey of these 5 years has been punctuated with many challenges & hurdles too. Biggest of them being the awareness among healthcare associates, lack of experts, patients from lower socio-economic background, high cost and lack of accessibility to clinical genetic testing. Numerous measures were taken to address these and many other challenges - the first of them were the continuous knowledge sharing programs for healthcare associates & genetic counsellors, KOL on-boarding, network expansion for accessibility, cost reductions for affordability, great sense of customer centricity, new launches and brand campaigns.

Addressing these hurdles has helped healthcare associates and genetic counsellors in taking up clinical genetic testing as an important diagnostic criterion in addition to their conventional practice. This increased recommendation has considerably narrowed the demand and supply imbalance – an empirical objective that MedGenome aimed for.

This fantastic journey wouldn't have been possible without the trust of healthcare associates, genetics counsellor, relentless efforts of a passionate & ever-enthusiastic business team and the confidence of the Chairman & Board members.

I would like to take this opportunity to thank all the stakeholders – Colleagues, Business Associates, Collaborators, Partners and Investors for being a part of this scintillating journey. We promise to keep our performance & deliveries intact and aim at reaching even higher standards.

Highlights

Most Talked About

The News

EDGENOME NEWS JANUARY To APRIL 2019 MEDGENOME NEWS

ACTIA • CLARIA • PRIMA • Business • Research • Awards • Genetic Counselling • Health Care

1

ectrum

netic testing critical during family planning

January 2019 | News

ne national policy of rare diseases clearly acknowledges that over 80 percent of rare disease patients are affected by approximately 350 rare diseases.

MedGenome Labs, a genomics and clinical data driven diagnostics and drug discovery research company organized an education workshop in Bengaluru recently highlighting the importance of carrier screening before marriage. The workshop had sessions by Dr. VL Ramprasad, Chief Operating Officer, MedGenome Labs, Dr. Priya Kadam, Program Director, Non-invasive prenatal testing and Dr. Sheetal Sharda, Consultant Clinical Geneticist.

The workshop highlighted the importance and relevance of carrier genetic testing for couples in India.

2

Business Standard

Cancer genetics: Beyond hereditary cancer (Health Notes) (February 4 is World Cancer Day)

ALSO READ

Single gene loss may have made humans long-distance runners: Study

In a first, Kerala captive jumbos get own genetic IDs

Genomic study may help

The gene is a unit of inheritance of our DNA that determines our characteristics including physical, behavioural and clinical and the term 'hereditary' means passed from the genes of a parent to the child. In cancer genetics, often these terms are used interchangeably.

The majority of us have a perception of genetics in the

3

BioVoice

"Data-driven medicine will enable the discovery of new treatment options"

4

Overcoming our genetic destiny

Sam Santhosh

We are the products of our genes and the environment. It has never ceased to amaze me that all living things on earth have a single origin and share the same genetic code – what Francis Collins called 'The Language of Life'. I would argue that deciphering this code has been humanity's greatest scientific achievement till date. We are privileged to be alive at this point of the journey of our species when we can, not only read (sequence) our code but also edit it.

If we consider the evolution of life on earth, the heroes of this journey are the genes. All living organisms have just been vehicles for the genes and were strictly condemned to their genetic destiny. Typically, the genes would lose interest in any organism after it crossed its reproductive stage and except for rare quirks, most organisms age quickly after reproduction and live barely enough to get their offspring to self-sufficiency. Undoubtedly, the environment also played a big part in shaping the genes, but looking at our planet's history, the genes seemed to have wormed its way out of all-natural catastrophes till now.

5

Worried About Breast, Ovarian Cancer? Genetic Testing Could Help

India accounts for the third highest number of breast cancer and second highest number of ovarian cancer cases among women, globally. Also, three times more cases of familial breast and ovarian cancers are recorded in India, as compared to western countries. It is projected that cancer incidence in Indian women will increase to 250- 200 cases per lakh by 2025 (Globocan, 2018; ICMR, 2012). Mortality to incidence ratio is worst in India for breast and ovarian cancers with one in every 28 women likely to develop it during her lifetime and one in every two women diagnosed with it, succumbing to it.

1. Genetic testing critical during family planning - Biospectrum
   https://www.biospectrumindia.com/news/77/12671/genetic-testing-critical-during-family-planning.html
2. Cancer genetics: Beyond hereditary cancer (Health Notes) (February 4 is World Cancer Day) - Business Standard
   https://www.business-standard.com/article/news-ians/cancer-genetics-beyond-hereditary-cancer-health-notes-february-4-is-world-cancer-day-119020200112_1.html
3. Data-driven medicine will enable the discovery of new treatment options - Bio Voice
   https://www.biovoicenews.com/data-driven-medicine-will-enable-the-discovery-of-new-treatment-options/
4. Overcoming our genetic destiny - Deccan Herald
5. Worried About Breast, Ovarian Cancer? Genetic Testing Could Help - Quint
   https://fit.thequint.com/cancer/breast-ovarian-cancer-and-genetic-testing

MedGenome Connect

ACTIA Medical Genetics

ACTIA team in action during DMD Screening camp by MedGenome in association with Indian Muscular Dystrophy Society (Ahmedabad)

Prima Cancer Genetics

Dr. Vidya at the Annual Molecular Pathology Association of India Meeting at ACTREC Mumbai, 12-13 Jan, 2019

A very happy new financial year 2019-20 to you all!

They say when the going gets tough, the tough gets going! This was demonstrated by the ACTIA Business team members in the last lap of FY 2018-19. Despite festivals, conferences, less working days, the team was determined to clock 100% of their business objective, and the same was achieved as well, justifying the theme of Above & Beyond set for FY 2018-19.

ACTIA participated in 2 major conferences and 14 CMEs during these 3 months. Collectively, MedGenome has reached out to more than 1000 clinicians.

In addition to these events, outdoor camps also were organized at Hyderabad, Vijayawada and Ahmedabad, majorly for screening patients of Duchenne Muscular Dystrophy (DMD)

The business team is all the more geared up to enhance their performance and consolidate leadership in genomics during the new financial year also. This will be punctuated by focused CMEs in Tier 2 towns and improved coverage of both territories and customers.

The period between 1st Jan 2019 to 25th March 2019 was quite exciting and full of events for Team PRIMA. We participated in 5 important national across India which included the following:

- Annual Molecular Pathology Association of India Meeting at ACTREC Mumbai, 12-13 Jan, 2019
- 3rd International Paediatric Pathology CME at TMC Kolkata, 17-20 Jan, 2019
- Lymphocon 2019 at Kidwai Bangalore, 12-13 Jan, 2019
- 4th MOSCON- Molecular Oncology Society Conference at Delhi, 16-17Feb, 2019
- 5th International Conference on Primary Immunodeficiency Diseases at Mumbai, 9 -11 March, 2019

Our team of experts, i.e. Dr. Ramprasad, Dr. Vidya, Dr. Sakthivel, Dr. Shruti made our participation remarkable with their involvement. The visibility and awareness on PRIMA and its offerings was boosted further by sales team across cities in India. The major therapies touch-based through these engagement programs were Oncology, Haematology and Primary Immunodeficiency.

MedGenome Connect

Claria
Reproductive Genetics

When inquisitive minds come together...knowledge gets multiplied!
Discussion on scope of NIPT in Indian settings @Dwarka Society of Gynecologists

The last lap of FY 2018-19 was an exciting and productive one for CLARIA, as we participated in numerous doctor events. Overall, the participation was in 7 CMEs and the biggest conference for Gynecologists. AICOG at Bangalore. This ensured that we could touch base with more than 1500 clinicians.

CLARIA team is determined to intensify promotion and scale up business in the new financial year through continued participation in such doctor events, and conduct many doctor engagement activities.

The key agenda for CLARIA in FY 2019-20 will be to establish new offerings like KT, FISH and CMA in Tier 2 & 3 towns, improve prescriber base by participating in multiple doctor events in these cities, and drive KOL engagement programs in Metro and Capital cities. Stay connected for more updates and success stories.

Making a difference

MedGenome's Comprehensive testing covers the entire *HBB* gene for β-thalassemia

Amit & Akhila (name changed), a non-consanguineous couple with clinical indication of primary infertility consulted a leading gynaecologist in India. After investigation she found both with abnormal HPLC profiles for haemoglobin and suspected of having β-thalassemia trait and suggested the couple to undergo genetic testing at MedGenome Labs, Bangalore.

β-thalassemia is an inherited blood disorder that reduces the production of haemoglobin. Mutations in the *HBB* gene cause β-thalassemia. The *HBB* gene is responsible for the synthesis of a protein called beta-globin which is a component (subunit) of haemoglobin. Mutations in this gene can result in decreased (β+) or no (β0) β-globin production leading to autosomal recessive disorders like β-thalassemia and sickle cell anaemia. Approximately 20 mutations, including deletions, insertions, base substitutions and alternate splice variants, are known to be responsible for abnormal β-globin production in South-East Asians. Of these, del619bp, IVS1-5 G>C; nt 147, IVS1-1 G>T; nt 143, codon 8/9 (+G) and codon 41/42(-TTCT) are more prevalent in the Indian population.

At MedGenome Labs the couple were tested for mutations in the *HBB* gene. It was found that only wife was positive for 1 mutation, c.92+5G>G/C. The husband who was negative for any mutations was tested using MLPA to detect Deletions/Duplication in the *HBB* gene. MLPA Testing detected the presence of the 619 bp-deletion, β-thalassemia mutation in heterozygous state. This is one of the most common β-thalassemia mutations, comprising >50% of β-thalassemia in Asian Indian sub-populations.

The recurrence risk in this case is 25% chance of having a child with β-thalassemia major, 50% chance of the child being a carrier like the parents and 25% chance of the child being normal (with respect to inheriting either mutations/deletion from the parents).

Comprehensive screening of the complete *HBB* gene by two different methods helped identify the genetic defect in both parents. Hotspot testing only identifies specific mutations but can miss rarer or novel mutations, but MedGenome's comprehensive testing covers the entire *HBB* gene and can identify any such mutation or deletion/duplication. Parents who have symptoms, family history of the disorder, or are known carriers of the disease, can benefit from prenatal testing for mutations in this gene.

From our US office

This quarter we attended the prestigious Molecular Medicine Tri-Conference – which provided us a unique opportunity to showcase our Oncology Products and other Genomics services.

Since its debut in 1993, the annual Molecular Medicine Tri-Conference has become one of the world's leading international events in the field of drug discovery, development and diagnostics. The Tri-Conference unites an ecosystem of 3,700 innovative thinkers and thought leaders throughout biotech, pharma and academia from around the world.

Recently, we organised a symposium on genomics where two distinguished scientists presented a talk on recent trends in Sequencing technology. Dr. Anup Madan, Vice President, Strategic Alliance, of TwinStrand Biosciences spoke about “One-in-A-Million: Applications of Duplex Sequencing” while Dr. Joseph Pickrell, CEO, Gencove, spoke about “Low-pass sequencing for cost-effective and scalable genomics applications” at the symposium.

We were also at the AACR event from March 29 - Apr 3, 2019, which was held at Georgia World Congress Center, Atlanta, Georgia, USA. The mission of the American Association for Cancer Research is to prevent and cure cancer through research, education, communication, collaboration, funding, and advocacy.

Sneak peek into the world of science

Savita Jayaram, *Ph.D.*
Bioinformatics Scientist

Keshav Bhojak
Bioinformatics Analyst

Immune receptor repertoire profiling - applications for clinical diagnostics and therapeutics

by **Savita Jayaram**, *Ph.D., Bioinformatics Scientist;*
Keshav Bhojak, *Bioinformatics Analyst*

Introduction

It is a miracle of billion-years evolution that vertebrates, including us – the humans, are constantly thwarting attacks from an ever-expanding universe of foreign invaders such as bacteria, viruses and other pathogenic organisms throughout our lifetime. The miracle that makes this happen is our adaptive immune system, comprising of B and T cells, and a host of other regulatory cell-types that function as a central command to activate, mobilize and eventually suppress the army of rogue killers, till the threat is completely eliminated. The puzzle of how our immune system recognize new organisms/biomolecules that may not have existed when we were born was revealed by the work of Susumu Tonegawa and others who discovered that the recognition mechanism is mediated by a family of highly diverse immune receptors expressed by the cells of the adaptive immune system - B, T and antigen-presenting cells (APCs) (Figure 1). This diversity enables the immune system to identify and mount an attack against any foreign element invading from outside the body (bacteria, virus), or generated inside (tumor cells) protecting us from deadly diseases. It is estimated that there are 109 – 1011 unique B cell receptors and 106 – 108 T cell receptors and about 301 known human leukocyte antigen (HLA) proteins expressed by the APCs in healthy humans.

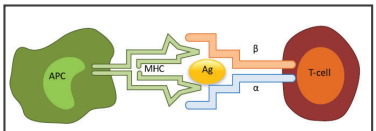

Figure 1: The figure shows the interaction between a T cell receptor and antigen in the context of MHC presented by an antigen presenting cell (APC).

Deeper insight into the immune-receptor diversity became possible with the advent of NGS and powerful bioinformatics and computational tools. Through these sequencing efforts, we know that two individuals, including monozygotic twins, do not share identical immune receptor repertoire, although each of us is capable of mounting an immune response against common pathogens indicating that there are enormous redundancy and plasticity in the recognition process. Further, the receptor repertoire undergoes significant expansion and contraction during diseases and these changes have led to the development of novel diagnostics in the area of autoimmune diseases.

In this essay, I will give an overview of the immune receptors and discuss how MedGenome is leveraging the NGS data of immune receptor repertoire and developing tools that will not only enhance the fundamental knowledge of how our immune system works but also how the diversity can be interrogated to discover biomarkers of productive immune response eliminating pathogens, versus adverse response targeting body's own cells leading to autoimmunity.

Immune repertoire diversity – how is it generated?

Immune receptors expressed by the B cells (B cell receptors, BCRs) and T cells (T cell receptors, TCRs) are formed during B cell development in the bone marrow and T cell development in the thymus. BCRs resemble the structure of an antibody with heavy and light chains and are membrane-bound (Figure 2A). TCRs are heterodimers of α and β polypeptide chains (αβ TCR), or γ and δ chains (γδ TCR). More than 90% of TCRs are αβ TCR (Figure 2B), while the rest are γδ TCRs. Both the receptors are created by recombining multiple gene segments residing at multiple genomic loci in the germline DNA that are brought within a coding sequence during B and T cell development. The gene segments, referred to as the variable (V) gene, the joining (J) gene and an additional diversity (D) gene (for heavy-chain and β-chain) followed by a constant (C) gene is added to all receptors. Figure 2A shows the assembly of a full-length BCR while Figure 2B shows the mechanism that generates a functional αβ TCR; following V(D)J recombination of the V, D, J and C genes. Receptor diversity arises at two levels. First, a combinatorial diversity in which recombination brings one of the 40-50 'V' gene segments with a 'D' and 'J' gene segments at the germline followed by splicing of the C gene at the RNA-level.

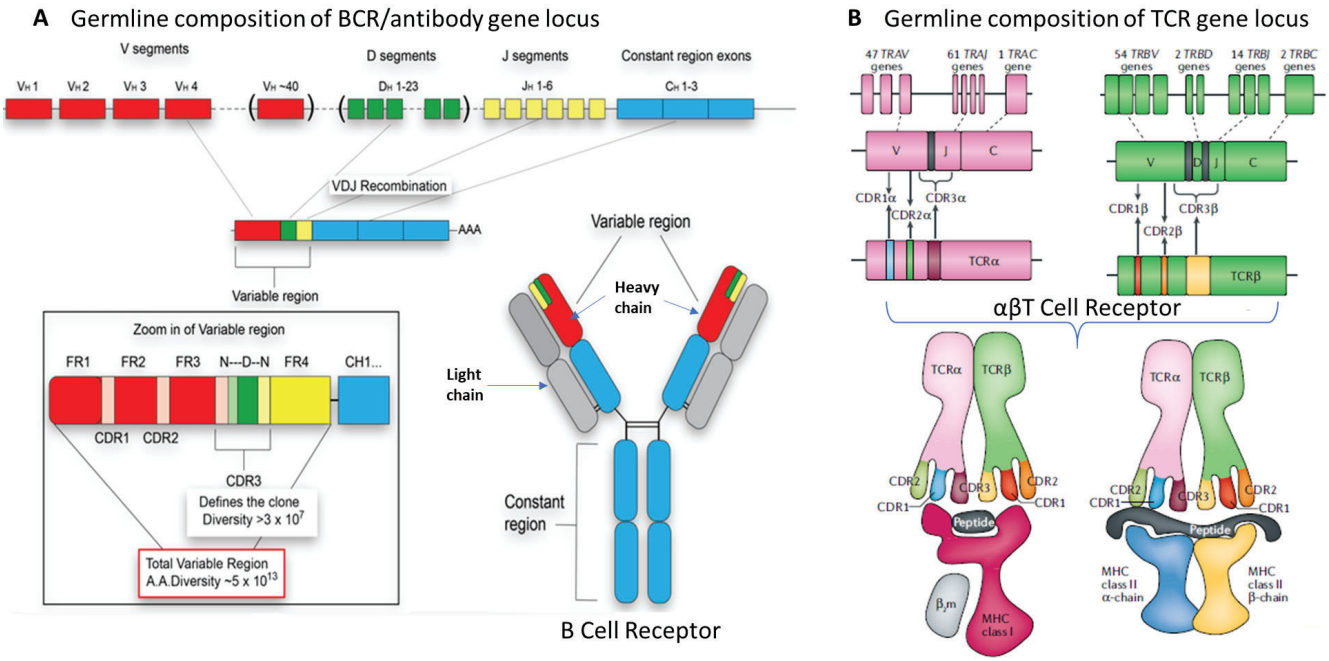

Figure 2: The right panel (A) shows the germline composition of an antibody gene locus with several V, D, J and C gene segments that come together to create a variable region following sequential gene recombination of V,D and J segments in the left panel (B) shows the analogous germline composition of TCR gene locus for alpha and beta chains that join to generate a fully functional αβ TCR that recognizes the peptide antigens in the context of MHC class I and class II proteins.

Figure adapted from https://www.bsse.ethz.ch/lsi/research/systems-immunology.html

The second level of diversity is introduced by random addition/deletion of nucleotides between gene segments (junctional diversity). Combinatorial and junctional diversity creates the final diversity of an individual's immune receptor repertoire and explains why two individuals cannot share identical repertoire. The sequence spanning the V-D-J junction is the 'hypervariable' segment, which is unique to each TCR-β chain and is called the complementarity determining region 3 (CDR3). The CDR3 region recognizes the antigen. The diversity of the TCR repertoire is analysed by enumerating the unique number of CDR3 sequences present in a T cell pool. Earlier experiments using bulk RNAseq data quantitated the enrichment of the CDR3 region. However, with the recent developments in single-cell RNA sequencing technology (scRNAseq), the transcriptomes of thousands of cells can be processed simultaneously, bringing an extra dimension to the analysis of TCRs from the scRNAseq experiments (Ref 2). Identification of each cell's unique TCRs using single cell technology now enables the pairing of α and β heterodimers that was not possible from bulk RNA sequencing. The enormous diversity of the TCR repertoire represents a major analytical challenge, which has led to the development of specialized software that aims to characterize the TCR repertoire in greater detail.

Applications of immune repertoire profiling

Immune repertoire profiling holds great potential not only for understanding the development of the normal immune response but also in providing insights into disease mechanisms leading to the development of new therapeutics and treatment modalities in infectious diseases, autoimmunity, and immuno-oncology. There is now increasing evidence that the BCR (and TCR) repertoires can serve as a proxy for aberrant immune response to many infections and autoimmune conditions, that can be monitored through patient blood/plasma, helping to gain a better understanding of their aetiology and progression (Figure 3).

Recent studies have demonstrated that TCR diversity enables monitoring and predicting response to immunotherapy drugs and the occurrence of immune-related adverse effects. Studies investigating tumor-immune interaction in cancer patients have shown that the circulating-TCR repertoire captures aspects of tumor-TCR repertoire with prognostic potential (Figure 4). Additionally, the immune repertoire

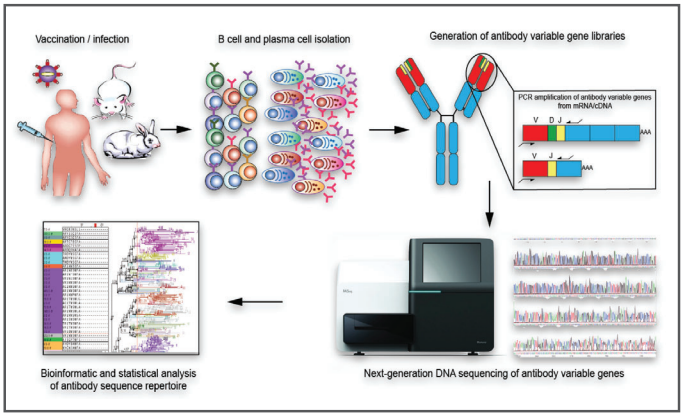

Figure 3: The figure shows B cells extracted from an infected individual and his associated B cell response leading to clonal expansion of antibodies present in blood/plasma. Sequencing the variable immunoglobulin chains followed by bioinformatic analysis of the antibody repertoire can provide a way to monitor the immune response.

data is being used to distinguish viral-driven cancers from non-viral ones, for precise tracking of vaccine-responsive T cell clones to enable more effective vaccine development. The diversity in the length of the CDR3 sequences has been linked to the T cell differentiation state - with longer CDR3 sequences enriched in antigen-naïve T cells than effector T cells.

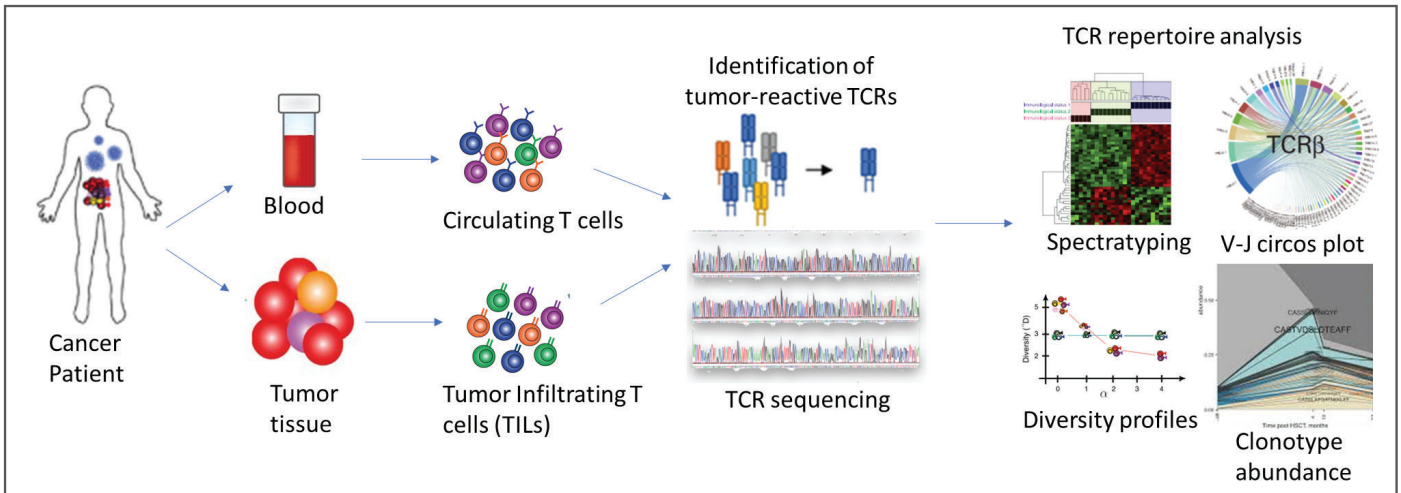

Figure 4: The figure shows T cells extracted from a cancer patient and the clonal expansion of tumor-reactive T cells from blood or TILs surrounding the tumor tissues. Sequencing the variable TCR chains followed by repertoire analysis can provide a way to monitor the immune diversity, clonotype abundance/frequencies and other parameters that can be used to monitor response to therapy or disease progression.

Despite variations in the clonotypic diversity between individuals, there are instances where many individuals share the same clonotypes referred to as shared “public” clonotypes (Figure 5). Given that these individuals also share a common disease suggest that the shared clonotypes may be directed towards a common disease-specific antigen

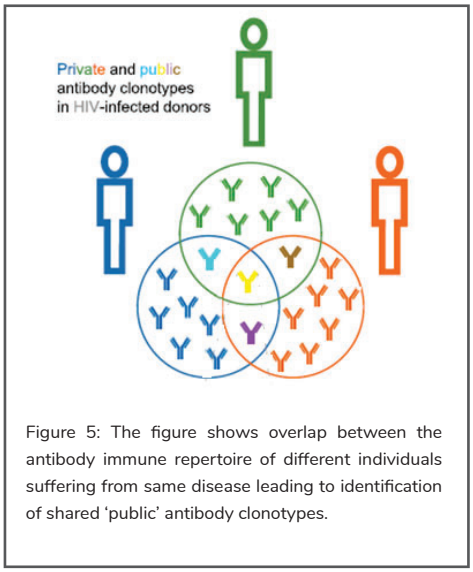

Figure 5: The figure shows overlap between the antibody immune repertoire of different individuals suffering from same disease leading to identification of shared ‘public’ antibody clonotypes.

Tools/resources for repertoire analysis

Given the complexity of immune repertoire data, there is a need to assimilate the right tools and algorithms to estimate both the amount and diversity of unique T cell clones that characterize the T cell repertoire of any individual. Currently, for TCR sequencing of samples, MedGenome offers NGS-based solutions using SMARTer® TCR Profiling Kit (Takara Bio USA Inc) and Single-cell V(D)J Immune Profiling solution (10X™ Genomics Inc.). Data generated using these kits are currently being analysed using CellRanger, MiXCR, and VDJtools (Reviewed in Ref 3). However, improved tools for accurately predicting the binding of TCR sequences with their cognate peptide-MHC complex out of a pool of non-binding TCRs are important areas of research. MedGenome has created additional software to integrate and work on top of these existing software solutions. Very similar to the genomic data explosion, we are now seeing a rapid accumulation of immune repertoire data in public repositories. This growing body of immune receptor data has tremendous utility in analyzing, annotating and interpreting the TCR and BCR sequence data. The Adaptive Immune Receptor Repertoire sequencing (AIRRseq) federated databases and repositories have created standardized representations of immune repertoire data to facilitate cross-dataset analysis and promote the reusability of AIRRseq data (Ref 4). The AIRR community, formed in September 2014, initiated the iReceptor resource to provide a unified gateway (http://ireceptor.irmacs.sfu.ca/) to query and access the AIRRseq TCR and IG data from different repositories (Figure 6). Since its inception, AIRRseq data has been growing at an exponential scale, currently providing access to 1.3 billion sequences and 879 samples.

Several computational and statistical analysis methods are being developed to resolve the complexity and deconvolute the dynamics of adaptive immunity from these large-scale AIRRseq data. MedGenome is part of an International consortium group which has been awarded a European/Canadian project grant to develop the next generation of the iReceptor platform referred to as the iReceptor-plus.

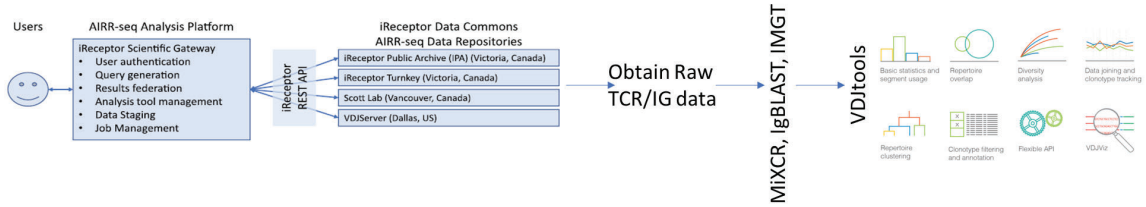

Figure 6: The figure shows iReceptor gateway to AIRRseq-repositories that can be queried to obtain raw TCR/IG data and further analysed using MiXCR, IgBLAST and VDJtools.

Conclusions

The scientific landscape is seeing an amalgamation of hypothesis-driven science and data-driven science that will have important ramifications for developing future therapeutics. The promising field of immune receptor repertoire is presented with new scientific and analytical challenges where currently no scalable solutions exist. With the exponential increase in genomic and transcriptomic data (both bulk and single cell) in addition to the rapidly accumulating immune receptor data, a scalable solution is expected with new developments in the areas of data aggregation, database management, cloud computing technologies and workflows for data integration along with scalability of computational tools for analysis. Although clear opportunities exist in analysing bigger volumes of data, it is important not to lose sight of the underlying biology. Dr. Sydney Brenner, a Nobel laureate in molecular biology commented, “There is a crisis these days. We are drowning in data and are still thirsty for more.” He said, “If we do not clearly define the problem, we won’t know what information is important.”

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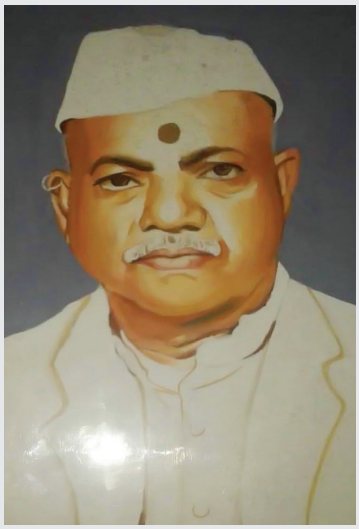
2. *Single cell T cell receptor sequencing: Techniques and future challenges. Simone et al. Front Immunol. (2018); 9:1638*
3. *Computational Strategies for dissecting the high-dimensional complexity of adaptive immune repertoires. Miho et al. Front Immunol. (2018); 9:244*
4. *AIRR Community Standardized Representations for Annotated Immune Repertoires. Heiden et al. Front Immunol. (2018); 9:2206*

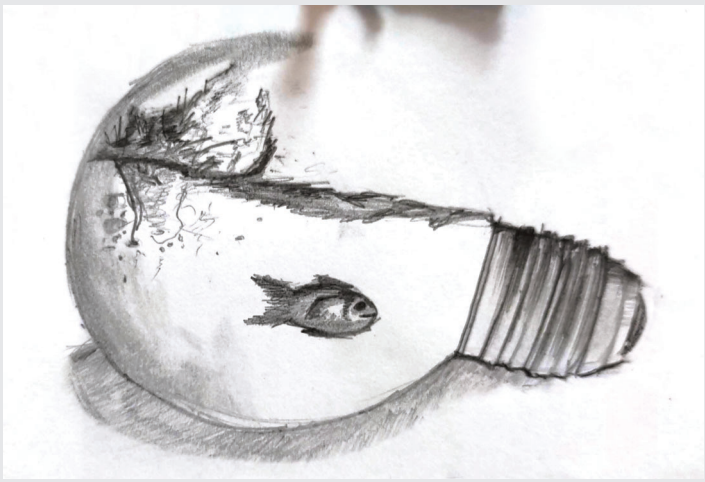
From our Colleague

Art meet Science

"Only art and science make us suspect the existence of life to a higher level, and maybe also instill hope thereof " by Ludwig van Beethoven



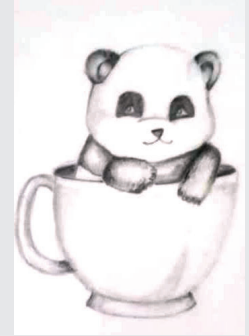
By Bhushan Mahajan, Software



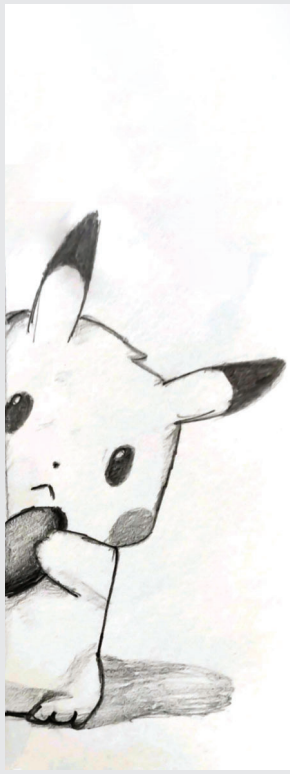
By Bhushan Mahajan, Software

By Netra Navadkar, Bioinformatics

By Bhushan Mahajan, Software



By Bhushan Mahajan, Software



By Bhushan Mahajan, Software

From our Colleague

Our employee's little Picasso :)

By: V Sucheta (11 Years)
DNA of Dr. Soumittra, Research

By: V Mahatej (4 Years)
DNA of Dr. Soumittra, Research

By: Rishikesh (9 Years)
DNA of Dr. Prachi Gadgil Fadnis, Bioinformatics

By: Rutuja (5 Years)
DNA of Dr. Prachi Gadgil Fadnis, Bioinformatics

From our Colleague

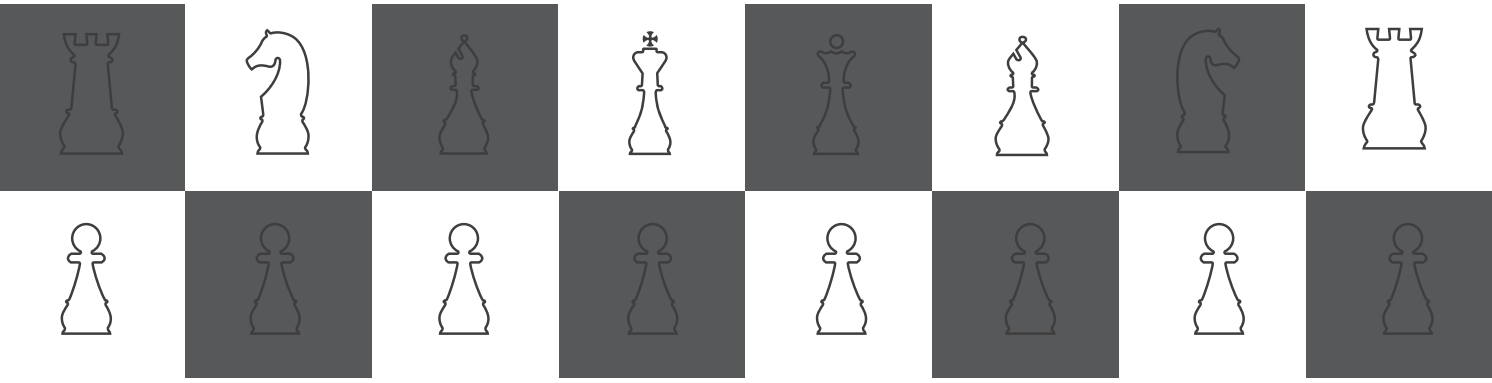
Prasanna Kumar S
Director

MedGenomians recently had an official permission to Chase the Queen on the chequered white and black board using all the grey matter of their brain. The enthusiasm and the interest towards this Royal Game of Chess was palpable. We should congratulate one and all who was involved and made this event a true success.

The celebrated strategic game of Chess was invented in India, can be traced back to around 1500 years, and then spread throughout the Asian continent. Chess made its way via the expanding Islamic Arabian Empire to Europe. Around 600 AD, the Arabic game shatranj developed from the Indian game chaturanga, becoming the first game identifiable as Chess. Until the end of the 15th century, Chess changed numerous times, survived sanctions by the religious groups as well as complete prohibitions from time to time. As always there is two side to a story – that side and this side, however often forgetting the true side. The true side is always immortal and the immortal Chess dominated the imagination of the masses, especially thanks to the contribution of Italians and Spaniards during the "Romantic Era of Chess". The rules of Chess changed numerous times until the 1880's (the romantic era of Chess). Chess slowly gained its competitive character and concrete rules, growing in popularity among the people.

While Chess has changed a lot since its invention, the basics of the game have remained recognizable throughout its long lifetime. From its ancient origins, Chess has evolved to appeal to modern players of all cultures and ages. With even conservative estimates placing the total number of Chess players today at half a billion people, there is no doubt that Chess is the king of board games.

The first official World Championship was hosted in 1886 where the Austrian-American Chess player William Steinitz became the first official world Chess champion in 1886. Steinitz's biggest contribution to Chess, however, was his advancement of the game's strategic understanding. Before the rise of Steinitz, until the middle of the 20th century, there were tendencies towards romantic Chess play, when players relied on tactics and extremely dynamic play – hopeful, and daring style full of reckless attacks. While some contemporaries called his ideas cowardly at first, those ideas earned Steinitz the nickname "the father of modern Chess."



My all-time favourite Bobby Fischer learned the rules of Chess at the age of six, and when he was 11 he “just got good,” according to Fischer himself. Six months after he turned 15, Fischer was a grandmaster, setting the record at the time for youngest GM ever. Fischer’s ascendancy peaked in 1972, when he defeated Boris Spassky and the Soviet Chess monolith to win the world championship in what is still considered the most famous Chess event ever. Three years later, though, Fischer disappeared from competitive Chess and public life, only to reappear 20 years later to beat Spassky in a rematch. It was like a nightmare come true again for Spassky. Fischer promptly withdrew from the spotlight once again, avoiding the Chess world until his death in 2008 at age 64 – the number of squares on a Chessboard.

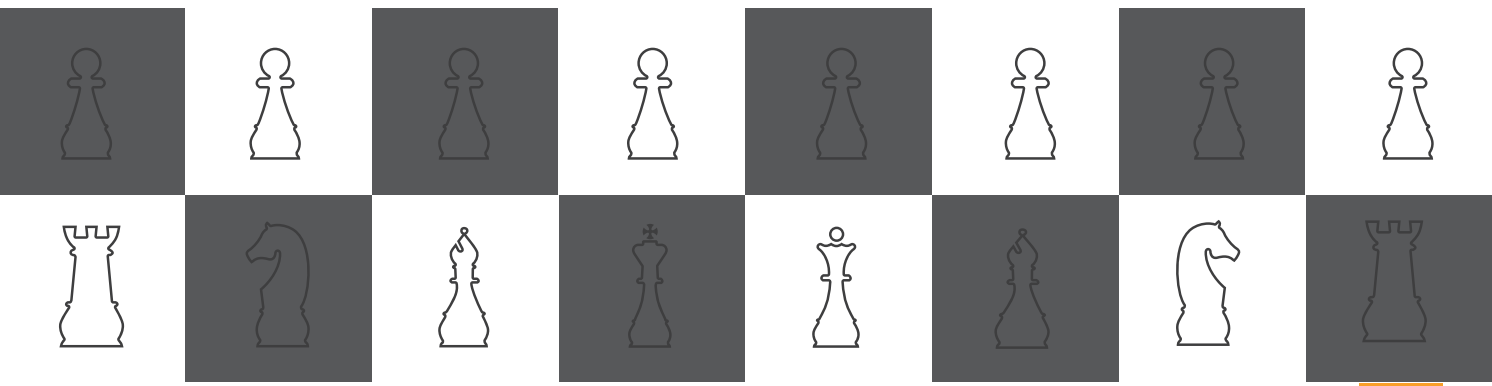
For us Indians, Vishwanathan Anand epitomized the zenith of Chess supremacy until the magnificent Magnus Carlsen era began. Like many other greats, Vishy was a child prodigy. He inspired a generation to take to Chess in India and made every middle class mother wish for a son like him thanks to his traditional demeanour. He will always be remembered as one of the greatest Indian ever (as of now the only Indian) to dominate the chequered board in the global arena.

Fischer and Kasparov are almost universally considered two of the strongest and most famous world champions of all time. However, the 20th century revolutionized Chess with the invention of databases, Chess engines and several methods for comfortable and efficient strategic preparations. IBM shocked the world defeating for the first time, the World Chess Champion, Garry Kasparov in 1997.

In 1989, the computer company IBM hired a team of Carnegie Mellon engineers to create a computer capable of beating the world Chess champion. Although Garry Kasparov defeated IBM's "Deep Thought" in 1989 and its next version in 1996, but in the 1997 rematch, “Deep Blue”, then capable of evaluating 200 million Chess positions per second, defeated Kasparov by a score of 3.5 to 2.5. Though Deep Blue made history, today's modern Chess engines running on ordinary computers could easily defeat Deep Blue. While they cannot calculate as many positions, today’s engines evaluate more efficiently and accurately.

Chess software today is far stronger than human Chess players. The human world champion Magnus Carlsen is rated 2877, while the best computer program, currently Stockfish is rated 3290.

Hearty **congratulations** to the **winner of CHASE THE QUEEN edition of 2019** at **MedGenome**, however in Chess often the player who goes after chasing the Queen leaving behind THE KING unprotected, ends up losing the Game. Protect your KING, the crown (your core) before chasing anything in life... and success will chase you sooner or later.



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Cross word puzzle

G L D N R N C K P C V D H U C E K J P C M T W R X C U K M Y
R E I O I S O O O R H Y O O G P N H Y U L E P T L V U U R X
N P N N W T E N L G O A A M M K H M E M R O I A V O I Y D D
A C E E K N R X D O I B R M I O A E J R U E N O R J K Q V B
V G T Y T E S O C I R N A G I N Z R N G E T B I S E P M O K
T Q H I W I D Y G H S B C B A N A Y Y O E D A R N I N K T D
P E I R I A C T N E R J L O I F O N G O T N I T E G S T I P
F M C X L L P C R D N O U I M L F A T O T Y E T I D T C S U
U T S O K L M V O A R B M N N P I X C C U Y P T Y O A Z A R
F T M S I E G Z B D I O A O C D L T C I O S P E I C N N O V
O I F G N L I V O S E T M S S T N E Y H D D E E I C D M A D
B X T J S E N S O E Q C S E E O I E T E R S O E O T S V Z G
U A I D W R B Q H X C R O S S S M O S E G O L M N P J F X S
Q G K K C G V C W A C H Y B R I D E N S D C M A I E F A O L
S R T R A I T S Q Q C P D D H G L M S N U O N O R N S L C F
I I W A T S O N L K L P K B J N P R O N J I M A S E A L R W
C B P Z B E U J U V R R G E N E S I O S B S U I M O N N S W
K O B V O H E O S P U G S E L F T B I M L Q S O N O M E T C
L N C L F P M B J G N Y X X X C I S O L S U S K I A P E D R
E U M W R R E P T V G I G J U R O C E T O O N T E Y N E R I
C C R T Z Y N D D P Z N X D Y R E C T G M O A M T E T C E C
E L P H X D D C N V H D O X B R R E Y O I C O D E I S V E K
L E L Y R J E N A R S R O I E E N Z R T I S O R R T I N E S
L I A M N C L S E N P E F N T N O H A L O O T E N S I P N E
A C S I P C I N I E D C I H U R C N P M L Y H A S L Y E N S
N A M N O S I E R W I S G P E F I E O B L N L E K T G I J R
E C I E O N T L L T O U W T V L R R S I I P C N O A N F O O
M I D T A O L T S T A U E M L W H Y M H A E A N T E G D T V
I D I U R E Z Y Y D P H F O A C B A H E R R E U D T D J E N
A M G P C K C C E Z Q T P Z Y K F K P B F G M A M V H P H F

Adenine
Allele
Amino acids
Blood Types
Cell reproduction
Chromosomes
Cloning
Codominant
Colorblindness
Cross-pollination
Cystic fibrosis
Cytosine
Daughter cells
Deoxyribonucleic acid
DNA
Dominant
Down Syndrome
Ethics
Family tree
Genes
Genetic code
Genetics
Genotype
Guanine
Heredity
Heterozygous
Homozygous
Hybrid
Incomplete dominance
Inherited
Karyotype
Meiosis
Mitosis
Mutagens
Mutation
Nitrogen bases
Nondisjunction
Parents
Pea plants
Phenotype
Plasmid
Probability
Proteins
Punnett square
Purebred
Recessive
Recombinant DNA
Replication
Ribonucleic acid
RNA
Self-pollination
Sex chromosomes
Sex-linked traits
Sickle cell anemia
Thymine
Traits
X chromosome
Y chromosome

Challenge:
The puzzle includes the last names of six people who have made contributions to the field of genetics. Who are they?

Kindly mail your answers by 15th May 2019 to editor@MedGenome.com. The first two people to answer the puzzles correct will be featured in the next edition of our newsletter.

Photo feature

Celebrations












MEDGENOME

Dear All

"Working hard for something we love is called passion" and at MedGenome we are all committed and passionate individuals. We present to you an opportunity to convey your emotions in the form of inspirational slogans and statements that will become part of our identity. These slogans should reflect the impact of what we at MedGenome do and how our work is making a difference to our society."

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The Last date for sending in your slogans is before

10
May 2019

Thanks & Regards
HR Team

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