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Genome Mapping Application in Diagnosis and Treatment of different Cancers

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Abstract--- *A wide range of cancer risk factors acts as mutagens and contributes to mutations in human body cells, some might cause carcinogenesis in cells, and then lead to the development of malignancies. Mutations occur in different cancers that can be in various forms, for instance, some contain gene amplification, but some have gene deletion. Doctors always seek to identify those essential genetic mutations in cancers for diagnosis and treatment, but those mutations increase as cancer cells develop over time, for example, metastasizing from primary sites to secondary sites. Genome mapping on cancers via different techniques are developed to be used as indicators of mutated genes, cancer genomes, therefore, provide new data for diagnosis and treatments of this disease, which assists pharmaceutical advancing on targeted therapy for treating specifically on gene mutations. Although genome mapping is helpful, there are ethical issues appear as well, which genome information can be considered as personal privacies. This review introduces mutation types in cancer as well as cancer risk factors, and how some of those mutations can be diagnosed by genome mapping, which focuses particularly on three methods in terms of their principles and how some of those are applied to diagnosis and drug development on four types of cancer.*

Keywords--- *Genome Mapping, Diagnosis and Treatment, Global Healthcare*

I. INTRODUCTION

Cancer is a wide-spread disease that is caused by several mutations of essential genes within a cell, causing 1 in 4 death in Europe in 2015 (Eurostat, 2019). The genetic change in the cancer cells can be caused by certain types of mutagens, which are substances that have a high potential of causing mutations in DNA. (Luch, 2019). Many factors affect the types of cancer including gender, with prostate cancer being high among men and breast cancer being high among women, due to several factors such as the composition of hormones (Dorak and Karpuzoglu, 2012). Other factors affecting cancer rate are exposure to carcinogens, lifestyle, and socioeconomic status.

Cancer cells should develop several mutations to have cancerous characteristics as they need to acquire the hallmarks of cancer in terms of self-sufficiency in growth signalling, insensitivity to antigrowth signals, evasion of apoptosis, limitless replicative potential, angiogenesis and metastasis (Hanahan and Weinberg, 2011). Despite all the progress which has been made, there are still challenges in cancer diagnosis and treatments because of many problems associated with characterizing cancer cells in laboratory and clinics (Zugazagoitia et al., 2016). Furthermore, cancer diagnosis and treatment can pose a financial burden on patients who are not supported by insurance or they have to pay for their medications as expensive drugs or services (de Souza and Wong, 2013). Therefore, cancer poses several challenges to global healthcare including financial burden.

II. MUTATIONS

Carcinogenesis is strongly related to the mutations on essential genes, which allows the cancer cells to

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metastasize. Tumor suppressing genes (Sherr, 2004) and protooncogenes (Todd and Wong, 1999) are two categories of genes that when they are mutated, can cause cells to become cancerous.

Normally, tumor suppressor genes and protooncogenes function to regulate cell growth and differentiation, and they lose this ability when they are mutated. Mutated cells might develop uncontrollable divisions as tumor suppressor genes are switched off as well as oncogenes develop to form proto-oncogene by several mechanisms such as gene amplification (Alitalo and Schwab, 1986; Todd and Wong, 1999).

As the cell division proceeds, an increasing number of mutations accumulate in the genome of the mutated cells, enabling cancer cells to acquire abilities such as invading the surrounding tissue and moving in the extracellular matrix by secreting proteases that enable them to degrade the extracellular matrix (Hanahan and Weinberg, 2011).

Also, metastasis occurs when cancer cells pass through the basement membrane and find their ways into the blood vessels and lymphatic system. Invasion-metastasis cascade consists of local invasion, intravasation, the transition of cancer cells through the bloodstream and lymphatic vessels, extravasation and colonization at a secondary tumor site (Hanahan and Weinberg, 2011).

When invasion and metastasis occur, tumor cells change from benign into malignant, and they become challenging to cure (Hanahan and Weinberg, 2011). For instance, some of the challenges for curing cancer cells are growth factor independent and anchorage-independent properties of cancer cells, allowing them to grow larger without the restriction of the surrounding tissues, turning them into a complex tissue consisting of many distinctive types of cells with different mutations which are called heterogeneity (Hanahan and Weinberg, 2011).

The mutation in cancer genes could be inherited or occur somatically (Genetics Home Reference, 2019b) as it is shown in Table 1.

Table 1: A Comparison of Two Types of Mutations Occurring in Cancer (Lakna, 2019)

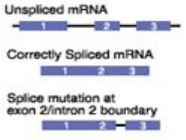
Germline	Somatic
Hereditary	Non-hereditary
Occur during gametogenesis	Occur at any time during an organism's life
Affect every cell in the body of the offspring	No effects on offspring

The germline mutations refer to the changes in the gene in the gametes of parents, which leads to the mutation in their offspring (Genetics Home Reference, 2019b). The germline mutation is more likely to occur in males as males' gametes undergo many more rounds of division than the female gametes during their lifetime, so more replicative associated mutations are introduced in males than females (Wilson Sayres and Makova, 2011).

Somatic mutations are related to the change of DNA sequence in somatic cells, which does not affect the offspring as they are not inherited (Griffiths et al., 2000) (Table 1).

Mutations are also categorized by the change of base pair sequence in DNA strands as it is shown in Table 2.

Table 2: Examples of different Types of Mutations (The Table is Adopted from Evolution, 2019)

Deletion	Genetic material is removed or deleted. A few bases can be deleted (as shown on the left) or it can be complete or partial loss of a chromosome (shown on right).	...TCGGAATCGC... ...TCGCGC... Ch. 13
Frameshift	The insertion or deletion of a number of bases that is not a multiple of 3. This alters the reading frame of the gene and frequently results in a premature stop codon and protein truncation.	...ACT TTT CAT AGT... ...Thr Phe His Ser... ...ACT TTT TCA TAG T... ...Thr Phe Ser Stop
Insertion	When genetic material is put into another region of DNA. This may be the insertion of 1 or more bases, or it can be part of one chromosome being inserted into another, non-homologous chromosome.	...TTGAAAACGCTG... ...TTGAAAAACGCTG...
Missense	A change in DNA sequence that changes the codon to a different amino acid. Not all missense mutations are deleterious, some changes can have no effect. Because of the ambiguity of missense mutations, it is often difficult to interpret the consequences of these mutations in causing disease.	...ACT CAG AAC... ...Thr Gln Asn... ...ACT CGG AAC... ...Thr Arg Asn...
Nonsense	A change in the genetic code that results in the coding for a stop codon rather than an amino acid. The shortened protein is generally non-function or its function is impeded.	...ATA CGA GCT... ...Ile Arg Ala... ...ATA TGA GCT... ...Ile Stop
Point	A single base change in DNA sequence. A point mutation may be silent, missense, or nonsense.	...CGTAATCCTCGA... ...CGTAGTCCTCGA...
Silent	A change in the genetic sequence that does not change the protein sequence. This can occur because of redundancy in the genetic code where an amino acid may be encoded for by multiple codons.	...TTC TGT AGT GGT... ...Phe Cys Ser Gly... ...TTC TGC AGT GGT... ...Phe Cys Ser Gly...
Splice Site	A change in the genetic sequence that occurs at the boundary of the exons and introns. The consensus sequences at these boundaries signal where to cut out introns and rejoin exons in the mRNA. A change in these sequences can eliminate splicing at that site which would change the reading frame and protein sequence.	
Translocation	A structural abnormality of chromosomes where genetic material is exchanged between two or more non-homologous chromosomes.	

Gene Mapping

One of the most important tasks of clinicians is to locate the loci of cancer genes in the chromosomes for diagnosis of the mutations that have occurred in cancer cells, which can be later used for treatments (Hanahan and Weinberg, 2011). Identifying mutations causing cancer can be done by genome mapping, which is linking different mutations in the genome to cancer causation (Nakagawa and Fujita, 2018). Large scale or minor changes in the structure of the genome (Table 2) are often seen in cancer cells, and these changes can be traced to identify mutations causing cancer. Jones et al. (2015) suggested that cancer tumor genomes should be compared to genomes from noncancerous tissues from the patient so doctors can ensure any mutations found are only present in cancer cells and not in normal cells. In this respect, drugs that are designed to be targeted to those cancer genes can be developed. However, during changing from primary tumor to secondary tumor which is genetically different, translocation of cancer cells from primary sites to secondary sites over time increases difficulties of diagnosis and treatment of cancers (Qian, et al., 2017) ss more mutations involving anatomically diffuse localization in different organs and cytotoxic-resistant agents are present in secondary tumors (Qian, et al., 2017). So, genome mapping provides scientists and clinicians with a novel way to search genetic mutations in cancer tumors, including copy-number alternations, germline mutation, epigenetic alternations and somatic mutations (Nakagawa and Fujita, 2018).

Cancer Risk Factors

Internal risk factors such as mistakes in DNA replication can cause cancer. On the other hand, many external factors can cause mutations in DNA, which cause the cells to develop into cancer cells. External cancer risk factors can be divided into physical factors, chemical factors, and biological factors which are summarized in Table 3. Ultraviolet rays from sunlight are the primary source of mutations for skin cancer, such as melanoma (Armstrong and Kricker, 2001). Tobacco smoking can cause lung cancer because of more than sixty types of carcinogens contained in tobacco (NHS, 2016). Additionally, unhealthy diets which include free radicals in foods such as boiled oil can cause mutations in the DNA (Ali Moustafa Elkhateeb, 2017) and obesity are associated with various types of cancers (Cancer, 2019). Viruses such as human papillomavirus can be one major factor in some cancers like cervical cancer in women (Walboomers et al., 1999).

Table 3: Main Risk Factors of all Cancers in Developing Countries (Sloan and Gelband, 2007). HBV, Hepatitis B Virus; HCV, Hepatitis C Virus; HPV: Human Papillomavirus; BMI, Body Mass Index

Cancer Type (number of deaths)	*Main Risk Factors*	*Theoretical Minimum Exposure Distribution*
All cancers (~5 million cancer deaths)	Tobacco use	Zero exposure possible
	HBV and HCV	Zero exposure possible
	HPV	Zero exposure possible
	H. pylori	Zero exposure possible
	Low fruit and vegetable intake	600 grams/day fruit and vegetable intake for adults
	Alcohol use	Zero exposure possible
	Physical inactivity	At least 2.5 hours/week of moderate- intensity activity or equivalent (4,000 kilojoule /week)
	Overweight and obesity	BMI (weight/height^2) of 21
	Urban air pollution	7.5 μg/m^3 for particles with aerodynamic diameters <2.5 microns
		15 μg/m^3 for particles with aerodynamic diameters <10 microns
	Indoor smoke from cooking and heating	Zero exposure possible

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Genome Mapping and Targeted Therapy

The genome mapping locates oncogenes that are related to different mutated proteins which cause the loss of regulation in cells or promote the cells to divide rapidly (Hunter, 1984). By sequencing the DNA and locating the loci of those suspected genes, the genome mapping provides comprehensive analysis for potential targeted therapies. It has been suggested by Huang et al., (2014) that gene expression, micro-RNA expression, and DNA methylation, provides hundreds-of-thousands of data points that can be used to evaluate the inner-workings of human cells and tissues.

There are two particular kinds of "maps" utilized in genome mapping: hereditary maps and physical maps (Mader et al., 2007). The two maps are an assortment of hereditary markers and quality loci, and separations in the hereditary guide depend on the hereditary linkage data, for example, a family outline, however physical maps utilize genuine physical separations typically estimated in the quantity of base sets (NIH, 2019a).When cancer researchers map out the genome of a cancer tumor (sequencing) to look for mutations that may allow cancers to be treated with a medicine that specifically targets a mutation – a targeted therapy medicine (NIH, 2019b).

Target therapy is not the only method, but it is more specific than other therapies like chemotherapy, which are used to treat cancer patients by stopping different phases of the cell cycle (AMBOSS, 2019) as it is shown in Table 4. Drugs used during chemotherapy can affect all the fast-dividing cells in patients including the cancer cells, follicular cells, and epithelium cells, thereby causing side effects (Bagnyukova et al., 2010). Compared to chemotherapy, targeted therapy only focuses on the cancer cells as they carry the unique molecular target that no other cells carry, therefore not harming the normal cells in the body (NIH, 2019b).

Table 4: The Comparison of Two Types of Cancer Treatment, Targeted Therapy and Chemotherapy

Targeted therapy	*Chemotherapy*
Particularly toxic to cancer cells, they also damage healthy cells	block only the mutant form of the protein but do not interfere with the activity of the normal cells
Cytotoxic and Cytostatic	Cytotoxic
Manty are oral agents	Mostly intravenous, some oral agents

The concept of personalized medicine is introduced using the targeted therapy for different patients according to their personal medical history, physiological status and molecular characteristics of the tumors (Garassino, 2014). The drugs for targeted therapy can be monoclonal antibodies or small molecule inhibitors (Joo, et al., 2013) which can interfere specifically with certain proteins or genes in the cancer cells, for example by blocking the interaction of the signaling molecule with its receptor (NIH, 2019). The breast cancer drug Herceptin, for instance, blocks binding to the Her2 receptors and interferes with their out-of-control cell signaling, which are overexpressed genes in Her-2 positive breast cancer (Pray, 2019).

It was suggested a long time ago that genome mapping, including physical and genetic maps, can be applied to access the risk of people getting a particular type of cancer in the future (Baptista, 1995). The risk factors could be determined through genetic testing which only requires a piece of DNA from them which can be obtained from the saliva or blood, then amplification and purification of DNA *in vitro* are carried out for later probing with many complementary DNA strands to diagnose genetic mutations in different cancer genomes (Kurzawski et al., 2012). So, people with a high risk of developing certain types of cancers can be identified, and undergo a regular checkup

to diagnose potential cancers (Korde and Gadalla, 2009).

Therefore, genome mapping can identify specific mutations within cancer-causing genes, so the specific treatments like targeted therapy can be developed and used to cure cancer cells by designing chemicals that interfere with specific cell molecules or genes for carcinogenesis (Joo et al., 2013).

Genomic technologies involving mapping different genes on chromosomes have been developed to diagnosis genes involved in cancer. Genome mapping techniques such as Comparative genomic hybridization, SNP arrays, whole-exome sequencing, and whole-genome sequencing can be used to pinpoint genes that contribute to cancer formation (Ow et al., 2013). Focusing on specific genes allows clinicians and scientists to target therapy to the mutated gene, thereby, developing a comprehensive cancer treatment plan.

III. GENOME MAPPING METHODS

Comparative Genetic Hybridization (CGH)

Oncogene enhancement has been perceived to happen in powerful human malignant growths and they're customarily connected with the action of disease, which is a colossal component within the finding of human malignancy (Bagci and Kurtgöz, 2015). In a humdrum CGH estimation, absolute genomic DNA is separated from test and reference mobile populaces in the course of metaphases and differentially named with more than a few fluorescence particles (Pinkel and Albertson, 2005). A reference test is taken from typical cells, at that factor increments or diminishes in the energy proportion legitimately exhibit DNA reproduction number variety like oncogene enhancements within the genome of the experiment cells (Pinkel and Albertson, 2005). In precise, the CGH procedure utilizes the overall forces of fluorescence in quite a lot of colorations, to come to a decision the level of enhancement.

Cluster CGH was grown later with improvements, for illustration, the capacity to all of the whilst identify aneuploidies, erasures, duplications, or intensification of any locus spoke to on an exhibit (Theisen, 2008). Rather than making use of metaphase chromosomes, this system makes use of slides exhibited with little fragments of DNA because the pursuits for investigation, which suggests a much less measure of test is required for the determination (Lucito et al., 2003).

Single Nucleotide Polymorphism Cluster (SNP Array)

A solitary nucleotide polymorphism (SNP) is a variety at a solitary trouble in a DNA grouping (table 2) (Scitable, 2019). Except quiet transformations, one SNP that occurs on exons brings concerning the change in a single amino corrosive from distinctive peptide chain to one other amino corrosive, as the modified triplet on mRNA converts into another amino corrosive which subsequently reasons the difference in main, not obligatory, tertiary, and quaternary structure of proteins, therefore, the brand new proteins framed cannot play out the targeted ability of the first ones or come to be completely denatured (Kimchi-Sarfaty et al., 2007). As 20 million rationed single nucleotide types happen with a characterized illustration in the populace, a procedure including making use of such sorts to genotype persons was created (worldwide HapMap C, 2007). The innovation can decide 1 *10^6 SNPs one after a different by using making use of the DNA microarray stage, and not at all just like the CGH, it would not

require a reference scan (Wu at el., 2009). Plus, SNP displays can likewise be applied to appreciate polymorphisms in germline DNA associated with the threat of 2nd fundamental tumors, which infers the application in the direction of the germline hazard appraisal of patients (Wu at el., 2009).

Entire Exome Sequencing

The genome includes of two districts exomes and introns; exomes are areas of the DNA which might be deciphered into protein-coding mRNAs, whilst introns are locales that are not translated into protein-coding mRNAs and are expelled from the final transcript object in the course of mRNA progress (Robinson et al., 2011). One hundred eighty,000 exons exist in the human genome, which is produced from 20 megabases and yield for round 20,000 protein-coding traits (Robinson et al., 2011).

As malignancy cells can have intensified exome groupings, the reproduction quantity increases or misfortunes of exomic DNA are completed with the aid of utilising entire exome sequencing (Robinson et al., 2011). This process allows for varieties within the protein-coding subject of any first-class to be well-known, versus in only a chosen few traits. In view that most known changes that reason ailment happen in exons, complete exome sequencing is believed to be a trained process to distinguish possible ailment causing transformations (Genetics house Reference, 2019a).

IV. Genome Mapping in various Types of Malignant Progress

Bosom Disease

Bosom sickness is a average kind of malignant progress in ladies world wide. It is evaluated that 5%-10% of all bosom malignant growth cases in ladies in 2015 are linked to innate vulnerability given that of transformations in autosomal predominant qualities (Sheik et al., 2015); on this manner genome mapping can be utilized to assume the frequency of bosom disease amongst families. The ascending of articulation of express qualities might be primary throughout the time spent the pathogenesis of powerful tumors, and first-rate intensification as one mannequin in general exists within the bosom malignant growth cells (Kadota et al., 2009). Enhancement of oncogene had been discovered in bosom carcinoma via hereditary investigation (Kallioniemi et al., 1994), yet it's traditional that more transformations happen in bosom malignant development cells. The mapping of districts of the genome with improved DNA reproduction quantity used to be found through main the process for CGH) onto 5 bosom cell lines and 33 foremost tumors, which assisted with displaying that increased DNA replica number results up to 26 chromosomal subregions in various patients (Kallioniemi et al., 1994).

A case of this sort of procedure of oncogene initiation in bosom malignancy is that of HER-2 (human epithelial receptor 2), which is based on chromosome 17q and encodes a 185-kDa transmembrane tyrosine kinase development factor receptor (Yarden and Sliwkowski, 2001). As there are extended phases of the outflow of the human epidermal development factor receptor (HER)- 2 protein, because of intensification of the HER2 first-rate, every once in a while happens in bosom tumors (Goddard et al., 2012), CGH process is completed via mapping HER-2 (Arriola et al., 2008) as regarded in figure 1.

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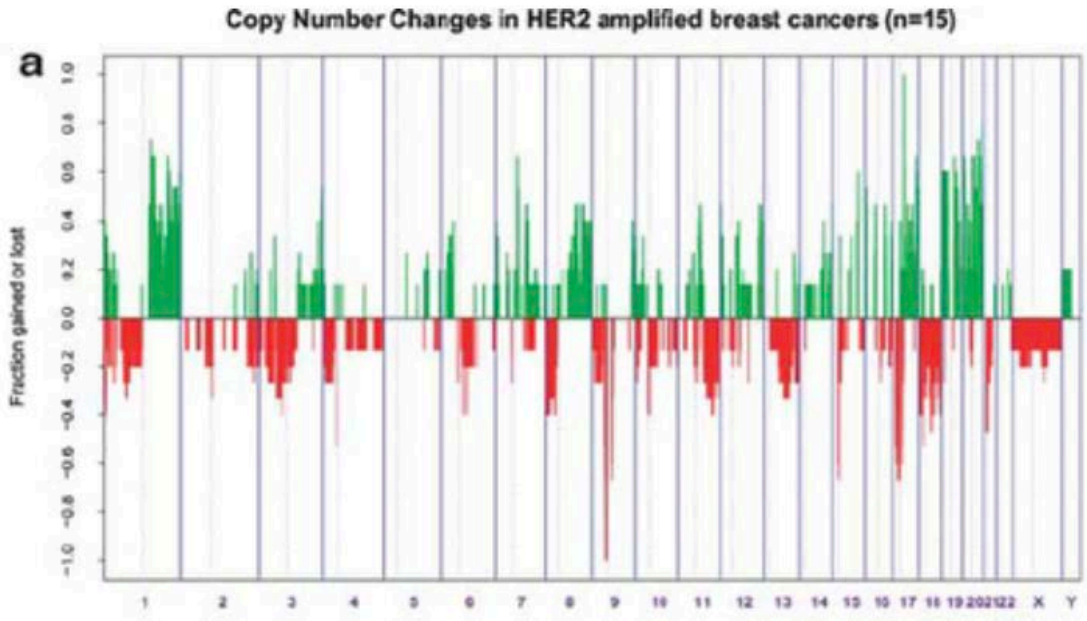

Figure 1: Frequency Plot of Chromosomal Gains and Losses in 15 HER2 -amplified Breast Cancers. The Figure is adopted from (Arriola et al., 2008)

Prostate Cancer

Prostate malignancy is the second most basic disease in men and the fourth most basic disease in general with progressively 1.3 million new yearly cases around the (World Cancer Research Fund, 2018). The CGH likewise assists with distinguishing the chromosomal awkward nature in the prostate malignant growth, worldwide high-goals cluster CGH examine to describe duplicate number changes in transitional hazard prostate disease (Ishkanian et al., 2009). The exploration did by (Bussemakers et al., 1999) expressed that an overexpressed cDNA, DD3 was recognized by contrasting the mRNA articulation examples of ordinary versus tumor tissue of the human prostate. It is one of the most prostate-malignancy explicit qualities, and DD3 could be utilized to be a dependable marker for the early finding of prostate disease and furthermore as a device for new treatment procedures. What's more, relative genomic hybridization (CGH) was applied onto cDNA microarrays so as to do genome-wide screens for areas of hereditary misfortune, including homozygous (complete) erasures that may speak to the conceivable area of tumor silencer qualities in prostate malignancy (Clark et al., 2003).

Lung Malignant Growth

Lung malignant growth is the most widely recognized disease in men and the third most regular disease in ladies around the (World Cancer Research Fund, 2018). Inquires about utilized genome mapping to discover the extensive characters of lung diseases, similar to little cell lung malignant growth, which is thought to begin from neuroendocrine cells in the bronchus (Champaneria et al., 2006) and is portrayed by quick expansion and early improvement of far reaching scattering (Han et al., 2014).

Squamous cell lung malignant growth, represents about 30% of all lung diseases (Harvard Health, 2017). Business innovation for catching and exome sequencing the DNA in the tumor was applied to the genome mapping

of squamous cell lung malignant growths (Rooney, Devarakonda and Govindan, 2013). By contrasting the tumor DNA and typical DNA to find the essentially changed qualities in which the desire model utilized for correlation depended on the specific estimated paces of explicit succession injuries (Rooney, Devarakonda and Govindan, 2013).

Pancreatic Malignant Growth

Pancreatic malignant growth represents about 3% of all diseases in the US and about 7% of all disease passings (Cancer.Net, 2019). Tumor cellularity in tests exposed to entire exome or - genome sequencing speaks to a realized obstruction in acquiring top notch information. The principal entire exome sequencing investigation of pancreatic malignant growth recognized countless changes and physical duplicate number adjustments that modify the capacity of many key oncogenes and tumor silencer qualities, including KRAS, TP53, SMAD4, and CDKN2A (Jones et al., 2008).

Pancreatic ductal adenocarcinoma (PDA) is a kind of exocrine pancreatic disease. It is the most widely recognized kind of pancreatic malignant growth – 95 out of 100 (95%) of every pancreatic disease are PDA (Pancreatic Cancer UK, 2018). Distinguishing various novel transformed qualities in PDA, with select qualities harboring prognostic importance. The change and duplicate number modifications every now and again included significant flagging pathways that add to tumor advancement and speak to restorative targets (Witkiewicz et al., 2015).

KRAS quality changes are seen in >90% of cases (Witkiewicz et al., 2015). In this manner, KRAS protein is an alluring medication target, in any case, absence of clear restricting locales has ruined pharmaceutical advancement (Ryan and Corcoran, 2018). One potential medication cooperation site is the place GTP or GDP ties. In any case, because of the remarkably high fondness of GTP or GDP for this site, it is far-fetched that medication like little particle inhibitors could rival GTP/GDP official (Holderfield, 2017).

V. END

Taking everything into account, different techniques, for example, aCGH, SNP cluster, and entire exome sequencing are utilized for identifying hereditary changes in the malignant growth genomes.

Cluster CGH is described by a high goals as its significant favorable position contrasted with traditional CGH; SNP exhibits use SNP as biomarker which helps researchers finding qualities that are related with illnesses; entire exome sequencing centers around qualities with protein articulation which can assist with recognizing oncogenes. Those techniques have added to working up the solid genome maps in various malignant growths, for example, lung, pancreatic, bosom and prostate diseases.

For the future improvement of genome mapping applications on malignant growth finding and medicines, these methods are bit by bit industrialized. All the more significantly, a key test is the moral and legitimate concerns related with the most creative advancements, including cell and quality treatment just as sequencing. This gives a specific favorable position to nations with less prohibitive laws, which are typically not western nations.

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REFERENCES

[1] Ali Moustafa Elkhateeb, Y. (2017). Impacts of speedy meals relating to Free Radicals and Antioxidants. *American Journal of Laboratory remedy*, [online] 2(6), p.156.

[2] AMBOSS. (2019). Chemotherapeutic operators – talents for medicinal understudies and medical professionals. [online] to be had at: https://www.Amboss.Com/us/information/Chemotherapeutic_agents [Accessed 20 Jul. 2019].

[3] Armstrong, B. What's more, Kricker, A. (2001). The study of sickness transmission of UV precipitated epidermis malignant progress. Diary of Photochemistry and Photobiology B: Biology, [online] 63(1-three), pp. Eight-18.

[4] Arriola, E., Marchio, C., Tan, D., Drury, S., Lambros, M., Natrajan, R., Rodriguez-Pinilla, S., Mackay, A., Tamber, N., Fenwick, k., Jones, C., Dowsett, M., Ashworth, A. What's more, Reis-Filho, J. (2008). Genomic investigation of the HER2/TOP2A amplicon in bosom malignancy and bosom disorder cell traces. *Research facility Investigation*, [online] 88(5), pp.491-503.

[5] Bagci, O. What's more, Kurtgöz, S. (2015). Intensification of phone oncogenes in strong tumors. *North American Journal of clinical Sciences*, [online] 7(eight), p.341.

[6] Balko, J., Stricker, T. Also, Arteaga, C. (2013). The genomic consultant of bosom malignant development: which streets lead to higher taken with treatments? *Bosom melanoma study*, [online] 15(four). Available at: https://www.Ncbi.Nlm.Nih.Gov/pubmed/23905624 [Accessed 28 Jul. 2019].

[7] Baptista, P. (1995). Access NCBI by means of the arena huge internet (WWW). Atomic Biotechnology, [online] 3(1), pp. Seventy five - seventy five.

[8] Bussemakers, M., van Bokhoven, A., Verhaegh, G., Smit, F., Karthaus, H., Schalken, J., Debruyne, F., Ru, N. Also, Isaacs, W. (1999). DD3: a brand new Prostate-express Gene, particularly Overexpressed in Prostate melanoma. Malignant growth study. [online] available at: https://cancerres.Aacrjournals.Org/ content material/fifty nine/23/5975 [Accessed 10 Aug. 2019].

[9] Ailment. (2019). Key statistics for Pancreatic melanoma. [online] available at: https://www.Cancer.Org/ malignant progress/pancreatic-sickness/about/key-records.Html [Accessed 28 Jul. 2019].

[10] Cancer.Internet. (2019). Pancreatic cancer - records. [online] on hand at: https://www.Cancer.Net/disorder types/pancreatic-malignant growth/insights [Accessed 2 Aug. 2019].

[11] Cancer.Net. (2019). The link between weight problems and cancer. [online] to be had at: https://www.Cancer.Web/exploring ailment care/recordings/after-cure-and-survivorship/interface amongst heftiness and-malignant development [Accessed 3 Jul. 2019].

[12] Champaneria, M., Modlin, I., Kidd, M. Also, Eick, G. (2006). Friedrich Feyrter: A precise mind in a Diffuse procedure. Neuroendocrinology, [online] eighty three(5-6), pp. 394-404.

[13] Clark, J., Edwards, S., Feber, A., Flohr, P., John, M., Giddings, I., Crossland, S., Stratton, M., Wooster, R., Campbell, C. Additionally, Cooper, C. (2003). Genome-huge screening for whole hereditary misfortune in prostate malignant development via near hybridization onto cDNA microarrays. Oncogene, [online] 22(8), pp. 1247-1252.

[14] Eurostat. (2019). World cancer Day: 1 out of 4 passings precipitated via malignant progress in the eu. [online] to be had at: https://ec.Europa.European/eurostat/net/items eurostat-news/ -/EDN-20170203-1 [Accessed 2 Jul. 2019].

[15] Development. (2019). Transformations. [online] on hand at: https://year10sciencewebsite.Weebly.Com/ mutations.Html [Accessed 2 Aug. 2019].

[16] Hereditary features residence Reference. (2019a). What are entire exome sequencing and entire genome sequencing? [online] to be had at: https://ghr.Nlm.Nih.Gov/preliminary/checking out/sequencing [Accessed 2 Aug. 2019].

[17] Hereditary characteristics home Reference. (2019b). What's a high-quality transformation and how do alterations occur? [online] to be had at: https://ghr.Nlm.Nih.Gov/groundwork/ mutations and disorders/genemutation [Accessed 18 Jul. 2019].

[18] Goddard, k., Weinmann, S., Richert-Boe, k., Chen, C., Bulkley, J. In addition, Wax, C. (2012). HER2 evaluation and Its impact on Breast cancer remedy choices. *Normal wellness Genomics*, [online] 15(1), pp.1-10.

[19] Griffiths, A., Miller, J., Suzuki, D. Moreover, Lewontin, R. (2000). A prologue to hereditary investigation. Seventh ed. New york, new york: Freeman.

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[20] Han, J., Lee, Y., Kim, B., Lee, G., Lee, S., Kim, E., Kim, H. Furthermore, Bhak, J. (2014). Whole genome investigation of a patient with opening time little mobile lung malignancy. *The Pharmacogenomics Journal*, [online] 14(6), pp.503-508.

[21] Harvard health. (2017). Squamous telephone Carcinoma of the Lung - Harvard health. [online] on hand at: https://www.Health.Harvard.Edu/a_to_z/squamous-telephone-carcinoma-of-the-lung a to z [Accessed 28 Jul. 2019].

[22] Holderfield, M. (2017). Endeavors to increase KRAS Inhibitors. Bloodless Spring Harbor perspectives in treatment, [online] eight(7), p.A031864. Available at: http://perspectivesinmedicine.Cshlp.Org/content material/8/7/a031864 [Accessed 2 Aug. 2019].

[23] Huang, W., Hsu, S., Huang, H., solar, Y., Chou, C., Weng, S. Furthermore, Huang, H. (2014). MethHC: a database of DNA methylation and satisfactory articulation in human malignant progress. Nucleic Acids study, [online] forty three (D1), pp. D856-D861.

[24] Ishkanian, A., Mallof, C., Ho, J., Meng, An., Albert, M., Syed, A., van der Kwast, T., Milosevic, M., Yoshimoto, M., Squire, J., Lam, W. Additionally, Bristow, R. (2009). Excessive-objectives showcase CGH acknowledges novel areas of genomic exchange in core hazard prostate malignancy. The Prostate, [online] 69(10), pp. 1091-1100.

[25] Jones, S., Anagnostou, V., Lytle, ok., Parpart-Li, S., Nesselbush, M., Riley, D., Shukla, M., Chesnick, B., Kadan, M., Papp, E., Galens, okay., Murphy, D., Zhang, T., Kann, L., Sausen, M., Angiuoli, S., Diaz, L. Also, Velculescu, V. (2015). Custom-made genomic examinations for malignancy transformation disclosure and translation. Science Translational treatment, [online] 7(283), pp.283ra53-283ra53.

[26] Jones, S., Zhang, X., Parsons, D., Lin, J., Leary, R., Angenendt, P., Mankoo, P., Carter, H., Kamiyama, H., Jimeno, A., Hong, S., Fu, B., Lin, M., Calhoun, E., Kamiyama, M., Walter, ok., Nikolskaya, T., Nikolsky, Y., Hartigan, J., Smith, D., Hidalgo, M., Leach, S., Klein, A., Jaffee, E., Goggins, M., Maitra, An., Iacobuzio-Donahue, C., Eshleman, J., Kern, S., Hruban, R., Karchin, R., Papadopoulos, N., Parmigiani, G., Vogelstein, B., Velculescu, V. Also, Kinzler, k. (2008). Middle Signaling Pathways in Human Pancreatic Cancers published via global Genomic Analyses. Science, [online] 321(5897), pp.1801-1806.

[27] Joo, W., Visintin, I. Also, Mor, G. (2013). Directed malignancy remedy – Are the occasions of predominant chemotherapy numbered?. Maturitas, [online] 76(four), pp.308-314.

[28] Kadota, M., Sato, M., Duncan, B., Ooshima, A., Yang, H., Diaz-Meyer, N., Gere, S., Kageyama, S., Fukuoka, J., Nagata, T., Tsukada, okay., Dunn, B., Wakefield, L. Also, Lee, M. (2009). Distinguishing proof of Novel Gene Amplifications in Breast melanoma and Coexistence of Gene Amplification with an Activating Mutation of PIK3CA. Malignancy research, [online] 69(18), pp.7357-7365.

[29] Kallioniemi, A., Kallioniemi, O., Piper, J., Tanner, M., Stokke, T., Chen, L., Smith, H., Pinkel, D., grey, J. Also, Waldman, F. (1994). Identification and mapping of more advantageous DNA successions in bosom malignant development with the aid of relative genomic hybridization. *Methods of the countrywide Academy of Sciences*, [online] ninety one(6), pp.2156-2160.

[30] Kimchi-Sarfaty, C., Oh, J., Kim, I., Sauna, Z., Calcagno, An., Ambudkar, S. Additionally, Gottesman, M. (2007). A "Quiet" Polymorphism in the MDR1 Gene alterations Substrate Specificity. *Science*, [online] 315(5811), pp.525-528.

[31] Korde, L. Also, Gadalla, S. (2009). Malignancy hazard comparison for the primary Care surgeon. Principal Care: Clinics in office practice, [online] 36(three), pp.471-488.

[32] Mader, S., Pendarvis, M. What's extra, Demott, S. (2007). McGraw Hill Biology. Ninth ed. Boston: McGraw-Hill bigger education, p.209.

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