Chapter 1 : Human Genome Project - Wikipedia

Traveling Around the Human Genome: An in Situ Investigation (Mbedicine/Sciences Sbelection): Medicine & Health Science Books @ www.nxgvision.com

The synthetic human genome could be around the corner The synthetic human genome could be around the corner By Graham Templeton on May 19, at 4: In biology, more than any other science, there is quite a lot of restraint. And that could bring up all new legal and ethical concerns, making the already muddy waters all the more treacherous. Usually, scientists who wanted a genome with particular characteristics would start with an adult genome and modify it by deleting, inserting, or changing a gene or genes within it. This genome can then be the basis for a single cell or, if put into a sperm or egg cell, to create an engineered animal. The human genome is more touchy, but we can genetically engineer cultures of human cells, and take individual human genes and put them into similar organisms to see what they do. A synthetic genome is different, because it is built entirely from scratch. You might be able to come in and add a few strokes here and there, perhaps even improve it a bit. But none of that implies that you could have painting the original in the first place, and you until you paint something yourself you can never really be sure you understand the techniques. Diving down into existing content is a great way to learn â€" but building up from nothing is the only way to master. Scientists can control DNA in amazing ways â€" but genome-length strands are still beyond current technology. In more concrete terms, scientists are starting to think about the prospect of literally building a human genome from individual bases of DNA; that is, designing and synthesizing a combination of genes that can support viable human cells, and theoretically allow proper development and functioning in the animal. In this case, our final load-out of genes is determined by some ungodly-long TXT file generated in a linoleum-floored computer lab. CRISPR allows direct editing of the human genome, making worry about direct synthesis a bit redundant. Right now, scientists are on the look-out for genetic freaks. They could create an array of many different gene-combo variants and do statistical analysis on the resulting cells to see which genes are necessary, in which patterns. Plus, creating genomes from scratch is a great way to learn how they work. The recent attempt to make the simplest possible genome is already paying dividends in terms of revealing the function of certain genes, even those that we thought we understood quite well. Creating a human genome from scratch would obviously be much more difficult from a mechanical perspective, just snapping together that much DNA without making mistakes or getting it all tangled up in itself. But unlike a hypothetical simple genome, we have the human genome available to use as a guide. The question of which of our genes are indispensable is an old one, and synthetic biology is the most plausible way to actually answer that question in the near future. However, many are worried about the safety of biological experiments involving human DNA, and in particular many observers worry about the potential to put human genetic material inside living cells, develop our genome in an embryo and grow a human being according to the complement of genes we designed on a word processor. How can scientists ethically justify experiments that could create horribly deformed humans? At its heart, this is a chemistry experiment. It has to do with snapping together nucleic acids, handling long chains of DNA so we can keep working with them even as they get unmanageably long, and keeping it all in working order until it gets inside the cell. What people are keying off is the very obvious question that follows this explanation: What this tech will do is make a lot of that sort of tinkering much more tantalizingly possible â€" and thus, in some direct sense, more probable to actually occur.

Chapter 2 : Human Genome Project | History, Timeline, & Facts | www.nxgvision.com

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History[edit] The Human Genome Project was a year-long, publicly funded project initiated in with the objective of determining the DNA sequence of the entire euchromatic human genome within 15 years. The fact that the Santa Fe workshop was motivated and supported by a Federal Agency opened a path, albeit a difficult and tortuous one, [9] for converting the idea into a public policy in the United States. Of particular importance in Congressional approval was the advocacy of Senator Peter Domenici , whom DeLisi had befriended. Congress added a comparable amount to the NIH budget, thereby beginning official funding by both agencies. The Project was planned for 15 years. A working draft of the genome was announced in and the papers describing it were published in February A more complete draft was published in , and genome "finishing" work continued for more than a decade. Ongoing sequencing led to the announcement of the essentially complete genome on April 14, , two years earlier than planned. The other regions, called heterochromatic , are found in centromeres and telomeres , and were not sequenced under the project. An initial rough draft of the human genome was available in June and by February a working draft had been completed and published followed by the final sequencing mapping of the human genome on April 14, Another proposed benefit is the commercial development of genomics research related to DNA based products, a multibillion-dollar industry. The sequence of the DNA is stored in databases available to anyone on the Internet. National Center for Biotechnology Information and sister organizations in Europe and Japan house the gene sequence in a database known as GenBank , along with sequences of known and hypothetical genes and proteins. Other organizations, such as the UCSC Genome Browser at the University of California, Santa Cruz, [28] and Ensembl [29] present additional data and annotation and powerful tools for visualizing and searching it. Computer programs have been developed to analyze the data, because the data itself is difficult to interpret without such programs. Techniques and analysis[edit] This section needs additional citations for verification. Please help improve this article by adding citations to reliable sources. Unsourced material may be challenged and removed. April Learn how and when to remove this template message The process of identifying the boundaries between genes and other features in a raw DNA sequence is called genome annotation and is in the domain of bioinformatics. While expert biologists make the best annotators, their work proceeds slowly, and computer programs are increasingly used to meet the high-throughput demands of genome sequencing projects. Beginning in , a new technology known as RNA-seq was introduced that allowed scientists to directly sequence the messenger RNA in cells. This replaced previous methods of annotation, which relied on inherent properties of the DNA sequence, with direct measurement, which was much more accurate. Today, annotation of the human genome and other genomes relies primarily on deep sequencing of the transcripts in every human tissue using RNA-seq. It is the combined mosaic of a small number of anonymous donors, all of European origin. The HGP genome is a scaffold for future work in identifying differences among individuals. Subsequent projects sequenced the genomes of multiple distinct ethnic groups, though as of today there is still only one "reference genome. There are approximately 22, [31] protein-coding genes in human beings, the same range as in other mammals. The human genome has significantly more segmental duplications nearly identical, repeated sections of DNA than had been previously suspected. It is considered a megaproject because the human genome has approximately 3. With the sequence in hand, the next step was to identify the genetic variants that increase the risk for common diseases like cancer and diabetes. So the National Institutes of Health embraced the idea for a "shortcut", which was to look just at sites on the genome where many people have a variant DNA unit. The theory behind the shortcut was that, since the major diseases are common, so too would be the genetic variants that caused them. The vectors containing the genes can be inserted into bacteria where they are copied by the bacterial DNA replication machinery. Each of these pieces was then sequenced separately as a small "shotgun" project and then assembled. The larger, , base pairs go together to create chromosomes. This is known as the "hierarchical

shotgun" approach, because the genome is first broken into relatively large chunks, which are then mapped to chromosomes before being selected for sequencing. Louis , and Baylor College of Medicine. Venter was a scientist at the NIH during the early s when the project was initiated. The Celera approach was able to proceed at a much more rapid rate, and at a lower cost than the public project because it relied upon data made available by the publicly funded project. Celera initially announced that it would seek patent protection on "only â€"" genes, but later amended this to seeking "intellectual property protection" on "fully-characterized important structures" amounting to â€" targets. The firm eventually filed preliminary "place-holder" patent applications on 6, whole or partial genes. Celera also promised to publish their findings in accordance with the terms of the " Bermuda Statement ", by releasing new data annually the HGP released its new data daily , although, unlike the publicly funded project, they would not permit free redistribution or scientific use of the data. The publicly funded competitors were compelled to release the first draft of the human genome before Celera for this reason. The scientific community downloaded about GB of information from the UCSC genome server in the first 24 hours of free and unrestricted access. Although the working draft was announced in June , it was not until February that Celera and the HGP scientists published details of their drafts. In February , at the time of the joint publications, press releases announced that the project had been completed by both groups. Only a few of many collected samples were processed as DNA resources. Thus the donor identities were protected so neither donors nor scientists could know whose DNA was sequenced. DNA clones from many different libraries were used in the overall project, with most of those libraries being created by Pieter J. One of these libraries RP11 was used considerably more than others, due to quality considerations. One minor technical issue is that male samples contain just over half as much DNA from the sex chromosomes one X chromosome and one Y chromosome compared to female samples which contain two X chromosomes. The other 22 chromosomes the autosomes are the same for both sexes. In the Celera Genomics private-sector project, DNA from five different individuals were used for sequencing. The lead scientist of Celera Genomics at that time, Craig Venter, later acknowledged in a public letter to the journal Science that his DNA was one of 21 samples in the pool, five of which were selected for use. It is anticipated that detailed knowledge of the human genome will provide new avenues for advances in medicine and biotechnology. Clear practical results of the project emerged even before the work was finished. For example, a number of companies, such as Myriad Genetics , started offering easy ways to administer genetic tests that can show predisposition to a variety of illnesses, including breast cancer , hemostasis disorders , cystic fibrosis , liver diseases and many others. For example, a researcher investigating a certain form of cancer may have narrowed down their search to a particular gene. By visiting the human genome database on the World Wide Web , this researcher can examine what other scientists have written about this gene, including potentially the three-dimensional structure of its product, its function s , its evolutionary relationships to other human genes, or to genes in mice or yeast or fruit flies, possible detrimental mutations, interactions with other genes, body tissues in which this gene is activated, and diseases associated with this gene or other datatypes. Further, deeper understanding of the disease processes at the level of molecular biology may determine new therapeutic procedures. Given the established importance of DNA in molecular biology and its central role in determining the fundamental operation of cellular processes , it is likely that expanded knowledge in this area will facilitate medical advances in numerous areas of clinical interest that may not have been possible without them. In many cases, evolutionary questions can now be framed in terms of molecular biology ; indeed, many major evolutionary milestones the emergence of the ribosome and organelles , the development of embryos with body plans, the vertebrate immune system can be related to the molecular level. Many questions about the similarities and differences between humans and our closest relatives the primates , and indeed the other mammals are expected to be illuminated by the data in this project. Genetic sequencing has allowed these questions to be addressed for the first time, as specific loci can be compared in wild and domesticated strains of the plant. This will allow for advances in genetic modification in the future which could yield healthier, more disease-resistant wheat crops. Ethical, legal and social issues[edit] At the onset of the Human Genome Project several ethical, legal, and social concerns were raised in regards to how increased knowledge of the human genome could be used to discriminate against people. Five percent of the annual budget was allocated

to address the ELSI arising from the project.

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Examples of human protein-coding genes. Alt splicing, alternative pre-mRNA splicing. Ensembl genome browser release 68, July Recently, a systematic meta-analysis of updated data of the human genome [22] found that the largest protein-coding gene in the human reference genome is RBFOX1 RNA binding protein, fox-1 homolog 1 , spanning a total of 2. Noncoding DNA Noncoding DNA is defined as all of the DNA sequences within a genome that are not found within protein-coding exons, and so are never represented within the amino acid sequence of expressed proteins. Numerous sequences that are included within genes are also defined as noncoding DNA. These include genes for noncoding RNA e. Protein-coding sequences specifically, coding exons constitute less than 1. The exact amount of noncoding DNA that plays a role in cell physiology has been hotly debated. Many DNA sequences that do not play a role in gene expression have important biological functions. Other noncoding regions serve as origins of DNA replication. Finally several regions are transcribed into functional noncoding RNA that regulate the expression of protein-coding genes for example [27] , mRNA translation and stability see miRNA , chromatin structure including histone modifications, for example [28] , DNA methylation for example [29] , DNA recombination for example [30] , and cross-regulate other noncoding RNAs for example [31]. It is also likely that many transcribed noncoding regions do not serve any role and that this transcription is the product of non-specific RNA Polymerase activity. Pseudogene Pseudogenes are inactive copies of protein-coding genes, often generated by gene duplication , that have become nonfunctional through the accumulation of inactivating mutations. Table 1 shows that the number of pseudogenes in the human genome is on the order of 13,, [32] and in some chromosomes is nearly the same as the number of functional protein-coding genes. Gene duplication is a major mechanism through which new genetic material is generated during molecular evolution. For example, the olfactory receptor gene family is one of the best-documented examples of pseudogenes in the human genome. More than 60 percent of the genes in this family are non-functional pseudogenes in humans. By comparison, only 20 percent of genes in the mouse olfactory receptor gene family are pseudogenes. Research suggests that this is a species-specific characteristic, as the most closely related primates all have proportionally fewer pseudogenes. This genetic discovery helps to explain the less acute sense of smell in humans relative to other mammals. The role of RNA in genetic regulation and disease offers a new potential level of unexplored genomic complexity. Within most protein-coding genes of the human genome, the length of intron sequences is to times the length of exon sequences Table 2. Regulatory DNA sequences[edit] The human genome has many different regulatory sequences which are crucial to controlling gene expression. Some types of non-coding DNA are genetic "switches" that do not encode proteins, but do regulate when and where genes are expressed called enhancers. The evolutionary branch between the primates and mouse , for example, occurred 70â€”90 million years ago. These sequences are highly variable, even among closely related individuals, and so are used for genealogical DNA testing and forensic DNA analysis. Among the microsatellite sequences, trinucleotide repeats are of particular importance, as sometimes occur within coding regions of genes for proteins and may lead to genetic disorders. Tandem repeats of longer sequences arrays of repeated sequences 10â€”60 nucleotides long are termed minisatellites. Mobile genetic elements transposons and their relics[edit] Transposable genetic elements , DNA sequences that can replicate and insert copies of themselves at other locations within a host genome, are an abundant component in the human genome. The most abundant transposon lineage, Alu, has about 50, active copies, [53] and can be inserted into intragenic and intergenic regions. Some of these sequences represent endogenous retroviruses , DNA copies of viral sequences that have become permanently integrated into the genome and are now passed on to succeeding generations. Mobile elements within the human genome can be classified into LTR retrotransposons 8. Genomic variation in humans[edit] Main articles: Human genetic variation and Human genetic clustering

Human reference genome[edit] With the exception of identical twins, all humans show significant variation in genomic DNA sequences. The human reference genome HRG is used as a standard sequence reference. There are several important points concerning the human reference genome: The HRG is a haploid sequence. Each chromosome is represented once. The HRG is a composite sequence, and does not correspond to any actual human individual. The HRG is periodically updated to correct errors and ambiguities. The HRG in no way represents an "ideal" or "perfect" human individual. It is simply a standardized representation or model that is used for comparative purposes. Measuring human genetic variation[edit] Most studies of human genetic variation have focused on single-nucleotide polymorphisms SNPs , which are substitutions in individual bases along a chromosome. Most analyses estimate that SNPs occur 1 in base pairs, on average, in the euchromatic human genome, although they do not occur at a uniform density. Thus follows the popular statement that "we are all, regardless of race , genetically For example, a much larger fraction of the genome is now thought to be involved in copy number variation. The genomic loci and length of certain types of small repetitive sequences are highly variable from person to person, which is the basis of DNA fingerprinting and DNA paternity testing technologies. The heterochromatic portions of the human genome, which total several hundred million base pairs, are also thought to be quite variable within the human population they are so repetitive and so long that they cannot be accurately sequenced with current technology. These regions contain few genes, and it is unclear whether any significant phenotypic effect results from typical variation in repeats or heterochromatin. Most gross genomic mutations in gamete germ cells probably result in inviable embryos; however, a number of human diseases are related to large-scale genomic abnormalities. Down syndrome , Turner Syndrome , and a number of other diseases result from nondisjunction of entire chromosomes. Cancer cells frequently have aneuploidy of chromosomes and chromosome arms, although a cause and effect relationship between aneuploidy and cancer has not been established. Mapping human genomic variation[edit] Whereas a genome sequence lists the order of every DNA base in a genome, a genome map identifies the landmarks. A genome map is less detailed than a genome sequence and aids in navigating around the genome. The HapMap is a haplotype map of the human genome, "which will describe the common patterns of human DNA sequence variation. Researchers published the first sequence-based map of large-scale structural variation across the human genome in the journal Nature in May These variations include differences in the number of copies individuals have of a particular gene, deletions, translocations and inversions. SNP frequency across the human genome[edit] Single-nucleotide polymorphisms SNPs do not occur homogeneously across the human genome. In fact, there is enormous diversity in SNP frequency between genes, reflecting different selective pressures on each gene as well as different mutation and recombination rates across the genome. However, studies on SNPs are biased towards coding regions, the data generated from them are unlikely to reflect the overall distribution of SNPs throughout the genome. Each column represents a 1 Mb interval; the approximate cytogenetic position is given on the x-axis. Clear peaks and troughs of SNP density can be seen, possibly reflecting different rates of mutation, recombination and selection. Changes in non-coding sequence and synonymous changes in coding sequence are generally more common than non-synonymous changes, reflecting greater selective pressure reducing diversity at positions dictating amino acid identity. Transitional changes are more common than transversions, with CpG dinucleotides showing the highest mutation rate, presumably due to deamination. Personal genomics A personal genome sequence is a nearly complete sequence of the chemical base pairs that make up the DNA of a single person. Because medical treatments have different effects on different people due to genetic variations such as single-nucleotide polymorphisms SNPs , the analysis of personal genomes may lead to personalized medical treatment based on individual genotypes. Personal genomes had not been sequenced in the public Human Genome Project to protect the identity of volunteers who provided DNA samples. That sequence was derived from the DNA of several volunteers from a diverse population. Thus the Celera human genome sequence released in was largely that of one man. Subsequent replacement of the early composite-derived data and determination of the diploid sequence, representing both sets of chromosomes , rather than a haploid sequence originally reported, allowed the release of the first personal genome. Since then hundreds of personal genome sequences have been released, [67] including those of Desmond Tutu , [68] [69] and of a

Paleo-Eskimo. The work was led by Manuel Corpas and the data obtained by direct-to-consumer genetic testing with 23andMe and the Beijing Genomics Institute. This is believed to be the first such public genomics dataset for a whole family. Personal genomics helped reveal the significant level of diversity in the human genome attributed not only to SNPs but structural variations as well. However, the application of such knowledge to the treatment of disease and in the medical field is only in its very beginnings. These knockouts are often difficult to distinguish, especially within heterogeneous genetic backgrounds. They are also difficult to find as they occur in low frequencies. Populations with a high level of parental-relatedness result in a larger number of homozygous gene knockouts as compared to outbred populations. Such populations include Pakistan, Iceland, and Amish populations. These populations with a high level of parental-relatedness have been subjects of human knock out research which has helped to determine the function of specific genes in humans. By distinguishing specific knockouts, researchers are able to use phenotypic analyses of these individuals to help characterize the gene that has been knocked out. A pedigree displaying a first-cousin mating carriers both carrying heterozygous knockouts mating as marked by double line leading to offspring possessing a homozygous gene knockout. Knockouts in specific genes can cause genetic diseases, potentially have beneficial effects, or even result in no phenotypic effect at all. Challenges to characterizing and clinically interpreting knockouts include difficulty calling of DNA variants, determining disruption of protein function annotation , and considering the amount of influence mosaicism has on the phenotype. It was found that individuals possessing a heterozygous loss-of-function gene knockout for the APOC3 gene had lower triglycerides in the blood after consuming a high fat meal as compared to individuals without the mutation. However, individuals possessing homozygous loss-of-function gene knockouts of the APOC3 gene displayed the lowest level of triglycerides in the blood after the fat load test, as they produce no functional APOC3 protein. Genetic disorder Most aspects of human biology involve both genetic inherited and non-genetic environmental factors. Some inherited variation influences aspects of our biology that are not medical in nature height, eye color, ability to taste or smell certain compounds, etc. Moreover, some genetic disorders only cause disease in combination with the appropriate environmental factors such as diet. With these caveats, genetic disorders may be described as clinically defined diseases caused by genomic DNA sequence variation. In the most straightforward cases, the disorder can be associated with variation in a single gene. For example, cystic fibrosis is caused by mutations in the CFTR gene, and is the most common recessive disorder in caucasian populations with over 1, different mutations known. However, since there are many genes that can vary to cause genetic disorders, in aggregate they constitute a significant component of known medical conditions, especially in pediatric medicine. Molecularly characterized genetic disorders are those for which the underlying causal gene has been identified, currently there are approximately 2, such disorders annotated in the OMIM database. In some instances population based approaches are employed, particularly in the case of so-called founder populations such as those in Finland, French-Canada, Utah, Sardinia, etc. The results of the Human Genome Project are likely to provide increased availability of genetic testing for gene-related disorders, and eventually improved treatment. Parents can be screened for hereditary conditions and counselled on the consequences, the probability it will be inherited, and how to avoid or ameliorate it in their offspring. As noted above, there are many different kinds of DNA sequence variation, ranging from complete extra or missing chromosomes down to single nucleotide changes. It is generally presumed that much naturally occurring genetic variation in human populations is phenotypically neutral, i.

Chapter 4 : Who was involved in the Human Genome Project? | Stories | www.nxgvision.com

The human genome: Dispelling the fogg travelling around the human genome (). By Bektkand Jokdak. Les Editions INSERM and John Libbey Eurotext: Paris. ix+pp. FF; $

In , James Watson and Francis Crick described the double helix structure of deoxyribonucleic acid DNA , the chemical compound that contains the genetic instructions for building, running and maintaining living organisms. Methods to determine the order, or sequence, of the chemical letters in DNA were developed in the mids. In , the National Institutes of Health NIH and the Department of Energy joined with international partners in a quest to sequence all 3 billion letters, or base pairs, in the human genome, which is the complete set of DNA in the human body. This concerted, public effort was the Human Genome Project. From the start, the Human Genome Project supported an Ethical, Legal and Social Implications research program to address the many complex issues that might arise from this science. All data generated by the Human Genome Project were made freely and rapidly available on the Internet, serving to accelerate the pace of medical discovery around the globe. The Human Genome project spurred a revolution in biotechnology innovation around the world and played a key role in making the U. In April , researchers successfully completed the Human Genome Project, under budget and more than two years ahead of schedule. There are now more than 2, genetic tests for human conditions. These tests enable patients to learn their genetic risks for disease and also help healthcare professionals to diagnose disease. At least biotechnology-based products resulting from the Human Genome Project are currently in clinical trials. Having the complete sequence of the human genome is similar to having all the pages of a manual needed to make the human body. The challenge now is to determine how to read the contents of these pages and understand how all of these many, complex parts work together in human health and disease. One major step toward such comprehensive understanding was the development in of the HapMap http: In , the third phase of the HapMap project was published, with data from 11 global populations, the largest survey of human genetic variation performed to date. HapMap data have accelerated the search for genes involved in common human diseases, and have already yielded impressive results in finding genetic factors involved in conditions ranging from age-related blindness to obesity. The tools created through the Human Genome Project continue to underlie efforts to characterize the genomes of important organisms used extensively in biomedical research, including fruit flies, roundworms, and mice. With the drastic decline in the cost of sequencing whole exomes or genomes, groundbreaking comparative genomic studies are now identifiying the causes of rare diseases such as Kabuki and Miller syndromes. Much work still remains to be done. Despite many important genetic discoveries, the genetics of complex diseases such as heart disease are still far from clear. Pharmacogenomic tests can already identify whether or not a breast cancer patient will respond to the drug Herceptin, whether an AIDS patient should take the drug Abacavir, or what the correct dose of the blood-thinner Warfarin should be. Based on a deeper understanding of disease at the genomic level, we will see a whole new generation of targeted interventions, many of which will be drugs that are much more effective and cause fewer side effects than those available today. NIH-supported access to high-throughput screening of small molecule libraries will provide academic researchers with powerful new research probes to explore the hundreds of thousands of proteins believed to be encoded by the approximately 25, genes in the human genome, and will provide innovative techniques to spur development of new, more effective, types of drugs. The increasing ability to connect DNA variation with non-medical conditions, such as intelligence and personality traits, will challenge society, making the role of ethical, legal and social implications research more important than ever. For additional information contact:

Chapter 5 : Images & Illustrations | Genome: Unlocking Life's Code

The exhibit was developed by the Smithsonian Institution and the National Institutes of Health's National Human Genome Research Institute. Mayo Clinic is the first medical center to sponsor the traveling exhibit.

Though the menace disappearedâ€”say, in the move from East Africa to North Americaâ€”the variant remained. These relic mutations could help explain how or why cancer evolved. Some genetic abnormalities influence how our bodies respond to medications, a field known as pharmacogenomics. One variant, for example, leaves people with HIV less tolerant to an anti-retroviral drug, a discovery that is changing treatment regimens across sub-Saharan Africa. Another messes with the breast cancer drug tamoxifen. The more diverse the genome, the higher the odds of finding mutations that may shape the choice of medication. In , he was an epidemiologist at the National Human Genome Center at Howard University and led the African branch of a project to collect genomes from around the world to uncover the scope of human genetic variation. Already, African scientists had a limited role, which stung Rotimi. In , while directing the Genome Center, he became the founding president of the African Society of Human Genetics, an organization formed to address this concern. A year later, geneticist Francis Collins, who led the Human Genome Project and now directs the National Institutes of Health NIH , attended the second meeting, held in Cairo, where the concern began morphing into an idea for an Africa-based genome project. Rising rates of cancer on the continent added further urgency. The prevalence of breast, prostate and cervical cancers is increasing there, partly due to lower mortality rate for infectious diseases and partly due to a shift toward a Westernized lifestyle. The problem is compounded by African patients being treated with drugs tested on non-African populations. Including African DNA in genetic research could ameliorate that issue. But Rotimi quickly realized that an Africa-centric effort had to do more than collect sequences and catalog SNPs. The rare appearance of funding for such research, coupled with the desperate need for better medical care, made practical application of the work a priority. And he was haunted by the specter of past research testing medicines and techniques on Africans but never helping them. It would be a massive research effort led by African scientists, located in African institutions and directly benefiting the African population. H3Africa would create parity between researchers there and in Europe and North America. A geneticist in Nigeria could compete with one at Harvard for fundingâ€”and win. Such an approach would avoid the disheartening patterns of the past and instead directly benefit African communities. In short, H3Africa would not just ensure that the genomics era landed squarely on the continent but that the kind of omission that characterized its early years would never happen again. A cervical cancer project is collecting genomes from 12, women in several countries to better understand the mutations that raise the risk of human papillomavirus triggering the malignancy. But the vision of a genetics project free from ethical dilemmas has not proved easy to achieve. Using money from non-African countries to fund research and the permitted inclusion of non- African collaborators in H3Africa-funded projects raises several concerns. About 10 years ago, for example, an international group of geneticists took DNA samples from the eldest members of four communities of San, hunter-gatherers in southern Africa with the oldest known lineages on Earth. Yagazie Emezi for Newsweek African scientists often end up with little involvement in the work using biological samples that they helped obtain. That history has left many researchers and would-be study participants skittish about genetic research. They worry that Africa will become an entire continent like Henrietta Lacks, the African-American cervical cancer patient whose family never knew that her cells had been exploited by scientists and widely used in medicine. This perspective may have some truth to it, but it also maintains the status quo. He wants to give African scientists the capability to stand on their own. Toward that end, lead investigators on any H3Africa project must be African, and ideally the collaborators as well. That requirement is building a new world of research capabilities across the continent, such as powerful computers to do bioinformatics research in Sudan; a repository in Uganda for storing DNA and generating a huge amount of data on the SNPs that protect against sleeping sickness; and equipment for fieldwork-documented hereditary neurological disorders in Mali, along with a laboratory to identify genetic mutations that increase risk and training for physicians there to educate

Malians about genetics and disease. H3Africa encourages collaboration among countries within Africa, but those with less advanced research capacity hesitate to assist more polished countries. In Ghana, some scientists at poorer institutions resent those at wealthier ones presenting work on shared samples without acknowledging their contribution. Others say they sometimes have more input on samples sent to New York than to South Africa. Just as with international collaborators, the idea of sending tissue samples across a border raises fears of exploitation and resentment about helping an economic competitor. H3Africa has tried to allay the concerns by letting scientists own their samples for longer. International standards of genetic research dictate that data be made publicly available. But H3Africa gives scientists 23 months of exclusivity, so they can study and publish their data without competition. Publications increase the profile of scientists, making them more attractive to funders, which in turn enriches their country. Biological samples are protected for even longer. Ethical guidelines for genetic researchâ€”these vary country to country, and H3Africa has its own strict regulationsâ€”say patients must give informed consent when they donate samples. But most languages across Africa lack words for technical terms like gene or biopsy. Ogechukwu Ikwueme, a breast cancer research coordinator, says patients need empathy to stick with care. One well-intentioned scientist created educational material using eye color to explain hereditâ€”this on a continent of people with brown eyes. Gender dynamics and community hierarchies also impede consent. These problems pervade scientific research everywhere. Rotimi often wrestles with questions about the women enrolling in his studies. The program is now in its last funding cycle, and its scientists will need to start competing for grant money with the rest of the world. They also need government support, which so far has been in short supply. Rotimi has appealed to the World Bank for help, and a new office for handling grant applications, to be peer-reviewed by Africans, is now operating out of Nairobi, Kenya. So far, country policymakers across sub-Saharan Africa have been reluctant to see the value of the work and agree to put more money toward science. Rotimi, who is now 61 and considers H3Africa a lifetime achievement, is well aware that politics could sabotage the whole effort. A study examining whether genome research has become more inclusive of African DNA since found only a 3 percent increase. Of the 2, genome-wide association studies completed at the time, just 19 percent included minorities.

Chapter 6 : Human Genome Project | www.nxgvision.com

The human genome is the complete set of nucleic acid sequences for humans, encoded as DNA within the 23 chromosome pairs in cell nuclei and in a small DNA molecule found within individual mitochondria.

See Article History Alternative Title: HGP Human Genome Project HGP , an international collaboration that successfully determined, stored, and rendered publicly available the sequences of almost all the genetic content of the chromosomes of the human organism, otherwise known as the human genome. The Human Genome Project HGP , which operated from to , provided researchers with basic information about the sequences of the three billion chemical base pairs i. The HGP was further intended to improve the technologies needed to interpret and analyze genomic sequences, to identify all the genes encoded in human DNA, and to address the ethical , legal, and social implications that might arise from defining the entire human genomic sequence. Timeline of the HGP Prior to the HGP, the base sequences of numerous human genes had been determined through contributions made by many individual scientists. However, the vast majority of the human genome remained unexplored, and researchers, having recognized the necessity and value of having at hand the basic information of the human genomic sequence, were beginning to search for ways to uncover this information more quickly. Because the HGP required billions of dollars that would inevitably be taken away from traditional biomedical research, many scientists, politicians, and ethicists became involved in vigorous debates over the merits, risks, and relative costs of sequencing the entire human genome in one concerted undertaking. Despite the controversy, the HGP was initiated in under the leadership of American geneticist Francis Collins , with support from the U. The effort was soon joined by scientists from around the world. Moreover, a series of technical advances in the sequencing process itself and in the computer hardware and software used to track and analyze the resulting data enabled rapid progress of the project. Deoxyribose sugar molecules and phosphate molecules form the outer edges of the DNA double helix, and base pairs bind the two strands to one another. Technological advance, however, was only one of the forces driving the pace of discovery of the HGP. Craig Venter , began to compete with and potentially undermine the publicly funded HGP. At the heart of the competition was the prospect of gaining control over potential patents on the genome sequence, which was considered a pharmaceutical treasure trove. Although the legal and financial reasons remain unclear, the rivalry between Celera and the NIH ended when they joined forces, thus speeding completion of the rough draft sequence of the human genome. The completion of the rough draft was announced in June by Collins and Venter. For the next three years, the rough draft sequence was refined, extended, and further analyzed, and in April , coinciding with the 50th anniversary of the publication that described the double-helical structure of DNA, written by British biophysicist Francis Crick and American geneticist and biophysicist James D. Watson , the HGP was declared complete. Science behind the HGP To appreciate the magnitude, challenge, and implications of the HGP, it is important first to consider the foundation of science upon which it was basedâ€”the fields of classical, molecular, and human genetics. Classical genetics is considered to have begun in the mids with the work of Austrian botanist, teacher, and Augustinian prelate Gregor Mendel , who defined the basic laws of genetics in his studies of the garden pea Pisum sativum. Mendel succeeded in explaining that, for any given gene , offspring inherit from each parent one form, or allele , of a gene. In addition, the allele that an offspring inherits from a parent for one gene is independent of the allele inherited from that parent for another gene. Each species has a unique set of chromosomes. For example, molecular genetics studies demonstrated that two alleles can be codominant characteristics of both alleles of a gene are expressed and that not all traits are defined by single genes; in fact, many traits reflect the combined influences of numerous genes. The field of molecular genetics emerged from the realization that DNA and RNA ribonucleic acid constitute the genetic material in all living things. In physical terms, a gene is a discrete stretch of nucleotides within a DNA molecule, with each nucleotide containing an A, G, T, or C base unit. It is the specific sequence of these bases that encodes the information contained in the gene and that is ultimately translated into a final product, a molecule of protein or in some cases a molecule of RNA. The protein or RNA product may have a structural role or a regulatory role, or it

may serve as an enzyme to promote the formation or metabolism of other molecules, including carbohydrates and lipids. All these molecules work in concert to maintain the processes required for life. Molecular genetics emerged from the realization that DNA and RNA constitute the genetic material of all living organisms. Studies in molecular genetics led to studies in human genetics and the consideration of the ways in which traits in humans are inherited. For example, most traits in humans and other species result from a combination of genetic and environmental influences. In addition, some genes, such as those encoded at neighbouring spots on a single chromosome, tend to be inherited together, rather than independently, whereas other genes, namely those encoded on the mitochondrial genome, are inherited only from the mother, and yet other genes, encoded on the Y chromosome, are passed only from fathers to sons. Using data from the HGP, scientists have estimated that the human genome contains anywhere from 20, to 25, genes. Advances based on the HGP Advances in genetics and genomics continue to emerge. Two important advances include the International HapMap Project and the initiation of large-scale comparative genomics studies, both of which have been made possible by the availability of databases of genomic sequences of humans, as well as the availability of databases of genomic sequences of a multitude of other species. The International HapMap Project is a collaborative effort between Japan, the United Kingdom, Canada, China, Nigeria , and the United States in which the goal is to identify and catalog genetic similarities and differences between individuals representing four major human populations derived from the continents of Africa, Europe, and Asia. The identification of genetic variations called polymorphisms that exist in DNA sequences among populations allows researchers to define haplotypes, markers that distinguish specific regions of DNA in the human genome. Association studies of the prevalence of these haplotypes in control and patient populations can be used to help identify potentially functional genetic differences that predispose an individual toward disease or, alternatively, that may protect an individual from disease. Similarly, linkage studies of the inheritance of these haplotypes in families affected by a known genetic trait can also help to pinpoint the specific gene or genes that underlie or modify that trait. Association and linkage studies have enabled the identification of numerous disease genes and their modifiers. In contrast to the International HapMap Project, which compares genomic sequences within one species, comparative genomics is the study of similarities and differences between different species. By comparing these sequences, often using a software tool called BLAST Basic Local Alignment Search Tool , researchers are able to identify degrees of similarity and divergence between the genes and genomes of related or disparate species. The results of these studies have illuminated the evolution of species and of genomes. Such studies have also helped to draw attention to highly conserved regions of noncoding sequences of DNA that were originally thought to be nonfunctional because they do not contain base sequences that are translated into protein. However, some noncoding regions of DNA have been highly conserved and may play key roles in human evolution. Impacts of the HGP Impact on medicine The public availability of a complete human genome sequence represented a defining moment for both the biomedical community and for society. In the years since completion of the HGP, the human genome database, together with other publicly available resources such as the HapMap database, has enabled the identification of a variety of genes that are associated with disease. This, in turn, has enabled more objective and accurate diagnoses , in some cases even before the onset of overt clinical symptoms. Association and linkage studies have identified additional genetic influences that modify the development or outcome for both rare and common diseases. For example, human genomic sequence information, analyzed through a system called CODIS Combined DNA Index System , has revolutionized the field of forensics , enabling positive identification of individuals from extremely tiny samples of biological substances, such as saliva on the seal of an envelope, a few hairs, or a spot of dried blood or semen. Indeed, spurred by high rates of recidivism the tendency of a previously convicted criminal to return to prior criminal behaviour despite punishment or imprisonment , some governments have even instituted the policy of banking DNA samples from all convicted criminals in order to facilitate the identification of perpetrators of future crimes. While politically controversial, this policy has proved highly effective. By the same token, innocent men and women have been exonerated on the basis of DNA evidence, sometimes decades after wrongful convictions for crimes they did not commit. Comparative DNA sequence analyses of samples representing distinct modern populations of humans have revolutionized the field of

anthropology. For example, by following DNA sequence variations present on mitochondrial DNA, which is maternally inherited, and on the Y chromosome, which is paternally inherited, molecular anthropologists have confirmed Africa as the cradle of the modern human species, Homo sapiens , and have identified the waves of human migration that emerged from Africa over the last 60, years to populate the other continents of the world. Databases that map DNA sequence variations that are common in some populations but rare in others have enabled so-called molecular genealogists to trace the continent or even subcontinent of origin of given families or individuals. Perhaps more important than helping to trace the roots of humans and to see the differences between populations of humans, DNA sequence information has enabled recognition of how closely related one population of humans is to another and how closely related humans are to the multitude of other species that inhabit Earth.

Chapter 7 : Human Genome | Evidence Design

Details on the traveling phase of the exhibit: The Science North traveling exhibit's team, in association with the Smithsonian's National Museum of Natural History and the National Institutes of Health's National Human Genome Research Institute, will handle the traveling phase of the exhibit Genome: Unlocking Life's Code.

When begun, HGP was dubbed "big science" comparable to placing human beings on the moon. History and goals The scientific goal was to map the genes and sequence human DNA. The primary motive was that which drives all basic science, namely, the need to know. The secondary motive was perhaps even more important, namely, to identify the four thousand or so genes that were suspected to be responsible for inherited diseases and prepare the way for treatment through genetic therapy. This would benefit society, HGP architects thought, because a library of DNA knowledge would jump start medical research on many fronts. Many early prophecies found their fulfillment. What was not anticipated was the competition between the private sector and the public sector. The ESTs located genes but stopped short of identifying gene function. A furor developed when researchers working with government money applied for patents on data that merely reports knowledge of what already exists in natureâ€"knowledge of existing DNA sequencesâ€"and this led to the resignation of James Watson b. Watson, who along with Francis Crick b. By Venter had established Celera Genomics with sequencing capacity fifty times greater than TIGR, and by June 17, , he concluded a ninety percent complete account of the human genome. It was published in the February 16, , issue of Science. Collins drew twenty laboratories worldwide with hundreds of researchers into the International Human Genome Sequencing Consortium, which he directed from his Washington office. Collins repudiated patenting of raw genomic data and sought to place DNA data into the public domain as rapidly as possible so as to prevent private patenting. His philosophy was that the human genome is the common property of the whole human race. Human DNA, as it turns out, is largely junkâ€"that is, Half of the junk DNA consists of repeated sequences of various types, most of which are parasitic elements inherited from our distant evolutionary past. Of dramatic interest is the number of genes in the human genome. At the time of the announcement, Collins estimated there are 31, protein-encoding genes; he could actually list 22, Venter could provide a list of 26,, to which he added an estimate of 10, additional possibilities. For round numbers, the estimate in stood at 30, human genes. This is philosophically significant, because when the project began in the anticipated number of genes was , It was further assumed that human complexity was lodged in the number of genes: So, confusion appeared when, nearing the completion of HGP, scientists could find only a third of the anticipated number. Confusion was enhanced when the human genome was compared to a yeast cell with 6, genes, a fly with 13, genes, a worm with 26, genes, and a rice cell with 50, genes. On the basis of the previous assumption, a grain of rice should be more complex than Albert Einstein. With the near completion of HGP, no longer could human uniqueness, complexity, or even distinctiveness be lodged in the number of genes. Collins began to speculate that perhaps what is distinctively human could be found not in the genes themselves but in the multiple proteins and the complexity of protein production. Culturally, DNA began to lose some of its magic, some of its association with human essence. The theology and ethics of HGP At the outset, HGP scientists anticipated ethical and public policy concerns; they were acutely aware that their research would have an impact on society and were willing to share responsibility for it. When in James Watson counseled the U. Department of Health and Human Services to appropriate the funds for what would become HGP, he recommended that three percent of the budget be allotted to study the ethical, legal, and social implications of genome research. Watson insisted that society learn to use genetic information only in beneficial ways; if necessary, the government should pass laws at both the federal and state levels to prevent invasions of privacy and discrimination on genetic grounds. Moral controversy broke out repeatedly during the near decade and a half of research. Shinn affirms that churches in the United States must be involved with genetic research and therapy. The churches have a particular concern for those who are hurt or whose faith has been shaken, as demonstrated by the long history of the churches in providing medical care. A team of molecular biologists, behavioral geneticists, theologians, and bioethicists monitored the first years of HGP research to articulate

theological and ethical implications of the new knowledge. Many religious and ethical issues eventually became public policy concerns. These are adumbrated below. When Watson recommended the establishment of ELSI, the first public policy concern was what he called privacy, here called genetic discrimination. An anticipated and feared scenario took the following steps. Disposition to muscular dystrophy , sickle-cell anemia, Tay Sachs disease, certain cancers, and numerous other diseases turned out to have locatable genetic origins. More knowledge is yet to come. When it comes, it may be accompanied by an inexpensive method for testing the genome of each individual to see if he or she has any genes for any diseases. Screening for all genetic diseases may become routine for newborns just as testing for phenylketonuria PKU has been since the s. The advantage is clear: Medical care from birth to grave could be carefully planned to delay onset, appropriately treat, and perhaps even prevent or cure genetically-based diseases. Despite the promise for advances in preventative health care, fear arises due to practices of commercial insurance. Insurance works by sharing risk. When risk is uncertain to all, then all can be asked to contribute equally to the insurance pool. Premiums can be equalized. Once the genetic disorders of individuals become known, however, this could justify higher premiums for those demonstrating greater risk. The greater the risk, the higher the premium. Insurance may even be denied those whose genes predict extended or expensive medical treatment. Some ethicists are seeking protection from discrimination by invoking the principles of confidentiality and privacy. This argument presumes that if information can be controlled, then the rights of the individual for employment, insurance, and medical care can be protected. There are grounds for thinking this approach will succeed. Legislative proposals during the s and early s seem to favor privacy. Other ethicists argue that privacy is a misguided cure for this problem. Privacy will fail, say its critics, because insurance carriers will press for legislation fairer to them, and eventually protection by privacy may slip. In addition, computer linkage makes it difficult to prevent the movement of data from hospital to insurance carrier and to anyone else bent on finding out. Most importantly, the privacy argument overlooks the principle that genome information should not finally be restricted. The more society knows, the better the health care planning can be. In the long run, what society needs is information without discrimination. The only way to obtain this is to restructure the employment-insurance-health care relationship. The current structure makes it profitable for employers and insurance carriers to discriminate against individuals with certain genetic configurationsâ€”that is, it is in their best financial interest to limit or even deny health care. A restructuring is called for so that it becomes profitable to deliver, not withhold, health care. To accomplish this the whole nation will have to become more egalitarianâ€”that is, to think of the nation itself as a single community willing to care for its own constituents. Given the divisiveness of the abortion controversy in the United States and certain other countries, fears arise over possible genetic discrimination in the womb or even prior to the womb in the petri dish. Techniques have been developed to examine in vitro fertilized IVF eggs as early as the fourth cell division in order to identify so-called defective genes, such as the chromosomal structure of Down syndrome. Prospective parents may soon routinely fertilize a dozen or so eggs in the laboratory, screen for the preferred genetic make up, implant the desired zygote or zygotes, and discard the rest. What will be the status of the discarded embryos? Might they be considered abortions? By what criteria does one define "defective" when considering the future of a human being? Should prospective parents limit themselves to eliminating "defective" children, or should they go on to screen for enhancing genetic traits such as blue eyes or higher intelligence? If so, might this lead to a new form of eugenics, to selective breeding based upon personal preference and prevailing social values? What will become of human dignity in all this? Relevant here is that the legal precedent set by Roe v. Wade would not serve to legitimate discarding preimplanted embryos. The Roman Catholic tradition has set strong precedents regarding the practice of abortion. The Second Vatican Council document Gaudium et spes states the position still held today: If it does, this may lead to recommending that genetic screening be pushed back one step further, to the gamete stage prior to fertilization. The genetic make up of sperm and ovum separately could be screened, using acceptable gametes and discarding the unacceptable. The Catholic Health Association of the United States pushes back still further by recommending the development of techniques of gonadal cell therapy to make genetic corrections in the reproductive tissues of prospective parents long before conception takes placeâ€”that is, gametocyte therapy.

Genetic determinism, human freedom, and the gene myth. Religious thinkers must deal not only with laboratory science but with the cultural interpretations of science, as well as public policy influenced by both. Even though molecular biologists withdraw from such extreme forms of genetic determinism, a cultural myth has arisen. Some commentators refer to it as the strong genetic principle ; others call it the gene myth. Genes, sin, crime, and racial discrimination. The belief in determinism promulgated by the gene myth raises the question of moral and legal culpability. Does a genetic disposition to antisocial behavior make a person guilty or innocent before the law? Over the next decade legal systems will have to face a rethinking of the philosophical planks on which concepts such as free will , guilt, innocence, and mitigating factors have been constructed. There is no question that research into the connection between genetic determinism and human behavior will continue and new discoveries will become immediately relevant to the prosecution and defense of those accused of crimes. The focus will be on the concept of free will , because the assumption of the Western philosophy coming down from Augustine that underlies understanding of law is that guilt can only be assigned to a human agent acting freely. The specter on the genetic horizon is that confirmable genetic dispositions to certain forms of behavior will constitute compulsion, and this will place a fork in the legal road: Either the courts declare the person with a genetic disposition to crime to be innocent and set him or her free, or the courts declare him or her so constitutionally impaired as to justify incarceration and isolation from the rest of society. The first fork would jeopardize the welfare of society; the second fork would violate individual rights. That society needs to be protected from criminal behavior, and that such protection could be had by isolating individuals with certain genetic dispositions, leads to further questions regarding insanity and race. The issue of insanity arises because the genetic defense may rely upon precedents set by the insanity defense.

Chapter 8 : Cancer Scientists Have Ignored African DNA in the Search for Cures

The Genome Project (HGP) was an international scientific research project with the goal of determining the sequence of nucleotide base pairs that make up human DNA, and of identifying and mapping all of the genes of the human genome from both a physical and a functional standpoint.

Your genome is a roadmap that can help you trace your ancestral past. Embark on a Genomic Journey and see yourself in a new way: Are you at risk for developing a hereditary cancer or rare disease? Do you have genetic factors that may affect the way you respond to certain medications? These are just some of the ways genetics may impact your health. Come learn about the genome â€" the complete set of instructions that help your body grow and function. Mayo Clinic is the first medical center to sponsor the traveling exhibit. With this knowledge, we can make better decisions about our health care. Journey through the genome Tour the three exhibit galleries to discover what a genome is, how it relates to medicine and health, and how it connects you to all of life on the planet, both past and present. Within each area, numerous topics are explored through the latest imagery on genomics, 3-D models, hands-on activities and videos. You can also attend special events to hear experts in genomics and medicine: These weekly presentations will feature scientific experts discussing many topics in genomic medicine, such as the connection between the bacteria in and on your body your microbiome and your health, the latest advances in prenatal testing, bioethics issues surrounding genomics and ways genomics help diagnosis rare diseases. Seniors in Medicine SMArt: This series will focus on genomics in medicine, covering topics related to aging and medications. It took nearly a decade, three billion dollars, and thousands of scientists to sequence the human genome in Discover how ongoing innovative technology is speeding up the process and cutting costs, as well as what this all means for DNA data management. Additional exhibits highlight a variety of topics: Basic concepts of genomic medicine: Created by the Mayo Clinic Center for Individualized Medicine, these educational videos highlight the wide range of areas where genomics research is being applied to improve medical care. Patients share their stories: These videos feature Mayo Clinic patients and their health care team, discussing how genomics helped diagnose and identify individualized treatments for a wide range of conditions. This video series features Mayo Clinic health care providers discussing what inspired them to pursue careers in genomic medicine. Geneticists, genetic counselors, biostatisticians and many more providers share their personal career journeys. Trait tree wall display: A large diagram guides visitors to identify four visible genetic traits unique to each person and features members of the local community. Attendees can stop at the photo kiosk, take their picture and see where they fit on the tree of shared genetic traits. Positive Exposure â€" The Spirit of Difference is a series of photographs by artist Rick Guidotti that seek to show the beauty of all people by photographing those living with genetic conditions. Beyond the Diagnosis displays commissioned paintings from artists around the world, each focusing on someone living with a rare genetic disease. Express yourself and celebrate what makes you unique. Learn more For more information about the exhibit, see the complete schedule of special events and presentations here. The Mayo Clinic Center for Individualized Medicine is sponsoring the exhibit with benefactor support. The conference is sponsored by the Mayo Clinic Center for Individualized Medicine and brings together precision medicine experts from Mayo Clinic and around the world to share how the latest genomic discoveries are advancing patient care.

Chapter 9 : The synthetic human genome could be around the corner - ExtremeTech

That is around the time that the official announcement of a human genome project was made in Biotechnology and genome education may be taught as individual lessons, units, special projects or in-school field trips, and even semester, yearlong and multi-year programs.