



BLOCKCHAINED CANNABIS DNA

THE INFORMATION CHAIN FOR
ADVANCED GROWERS AND REGULATORS

This document will provide an overview of how the cannabis industry can use DNA sequencing and blockchain technology to create a transparent supply chain that cultivators, dispensaries, regulators, and consumers can trust.

A blockchain-based genetic catalog of all cannabis varieties in a given market provides transparency to an opaque world of underground names and folklore medicine. We have the unique ability in time to build the most comprehensive cannabis tracking system in the world that will bring patient safety, manufacturer transparency, and regulatory comfort.

Such a system is attractive to regulators, because it delivers emergent incentives against diversion and counterfeiting. Blockchain-linked mobile phone applications could instantly verify legitimate material with QR code links to public strain data on Kannapedia.net.

Cannabis breeders and cultivators can also use genetic sequencing to accurately fingerprint their varieties and publish their genetic data to the Bitcoin blockchain. They can then use the information to defend against any future patents or file for their own patent.

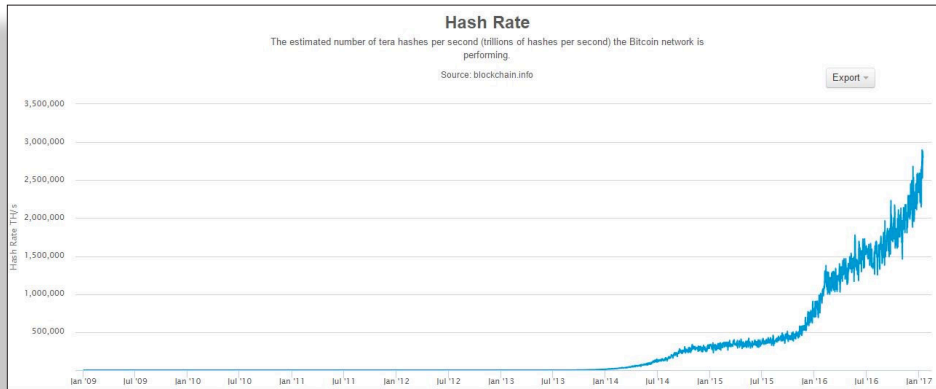


www.medicinalgenomics.com

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Why Blockchains?



Blockchains are global, transparent, hack-proof ledgers that are ideally suited for storing data that is valuable to many different collaborative and potentially competitive parties. As a result, blockchains present immutable ledgers that anyone in the world can view, and everyone can verify.

Bitcoin is largest and most trustworthy blockchain. The Bitcoin network is now 100 times larger the top 500 supercomputers combined¹. Google's computing power doesn't even match this Hashing power. As a result, there is not enough computational power on the planet to hack the Bitcoin network.

Due to this unique and clever design, Bitcoin has been the fastest-growing and best-performing global currency since its inception in 2008. The Bitcoin ledger is so trustworthy, society has parked more cash there than the market cap of PayPal, Netflix, or Goldman Sachs (\$98B and its more than doubling every year). This is the most trusted data store on Earth. Providing further evidence that the Bitcoin network will continue to grow is the fact that Nexus and others are planning to launch thousands of low earth orbit cube satellites to bring wifi access and cryptocurrency to every ocean and remote corner of the globe.

Blockchains are arguably the most significant invention in computer sciences in 50 years. This is the distributed architecture required to avoid future events like the hacking of the "MJ Freeway" servers that occurred in 2017². That single event nearly shut down the cannabis industry in entire states, forcing dispensaries to use paper-based order processing for several weeks.

To provide decentralized, disaster-resistant ledgers for the industry, blockchains are a modern requirement. Any other architecture is fragile or dangerous by design.

**BITCOIN
BY THE NUMBERS**

**NETWORK
100x
LARGER THAN THE TOP
500 SUPERCOMPUTERS
COMBINED**

**MARKET CAP
98B**

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Why DNA?

DNA information positively benefits consumers, growers, and regulators. There are over 560 compounds found in Cannabis and analytical labs are only measuring a few cannabinoids and less than 24 terpenes. Many of these unmeasured compounds are therapeutic antioxidants like Anthocyanins and Flavonoids³. Quantitative analytical techniques and standards for all 560 compounds do not exist in 2017⁴.

We do not anticipate affordable, validated, full-profile analytical assays existing in the next decade, if ever. As a result, the existing chemotypes are really only capturing less than 10% of the chemical and potential medicinal complexity in the plant. These really need to be regarded as “micro-chemotypes” given the large blind spots inherent in the current chemotyping methods.

To fill in this void, the best proxy for this unmeasured chemical complexity in the plant is the plants’ own genome. Using genomics we can record the chemical potential of the plant and provide a tool to identify other clonal plants that encode the same potential. This is very valuable information, and it greatly complements the existing cannabinoid and terpenoid measurements commonly collected today. Only with both datasets can we guarantee consistency for patients looking for reproducibility.

Nature versus Nurture

While the genetics can be coached to express varying concentrations of compounds, the relative ratios of the key chemotypic genes, like THCA and CBDA, are usually genetically determined. As an example, there are no known agricultural methods to make a CBD-dominant strain become a THC-dominant strain via environmental conditions. These critical chemotypes are governed by gene knock outs in their respective enzymatic synthases (CBDA Synthase and THCA Synthase)^{5-7 8}.

For this reason we tend to see THCA dominant Type I plants, THCA:CBDA hybrid Type II plants, and CBDA dominant Type III plants. We also tend to see the cannabis industry rely on genetic cloning of plants to maintain consistent chemotype expression. Tracking genetic cloning events and micro-chemotypes are the core tools of experienced breeders.

DID YOU KNOW?

There are over 560 compounds found in Cannabis, yet analytical labs typically measure fewer than 6 cannabinoids and 24 terpenes.

“There are no known agricultural methods to make a CBD-dominant strain become a THC-dominant strain via environmental conditions because these critical chemotypes are governed by gene knock outs in their respective enzymatic synthases”

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Breeding is complex

Since cannabis genomes are 10 fold more variable than human genomes, sibling seeds are not guaranteed to produce similar chemotypes. A given cannabis strain has the capacity to cross with other strains that are very different from itself. This is the near equivalent of humans and chimpanzees being capable of having productive offspring. As a result, many strains that are siblings of “Blue Dream” should not be assumed to deliver the same chemotype.

The capacity to genetically differentiate clones from siblings is a valuable breeding tool for growers, patients, and regulators. The capacity to differentiate them is directly related to the amount of sequencing one performs. Low information sequencing cannot discern closely related siblings from backcrossed parents or clones.

DNA is a better fingerprint

DNA is the only barcode that ends up in the consumer’s hand whether the sample is mislabeled, counterfeited, or diverted. RFID tags are complementary tracking tools but not surprisingly are never found on diverted or counterfeited material.

While many testing labs have suggested the use of chemotypes as a fingerprint for a strain, this is a misuse of the term fingerprint. The current micro-chemotyping tools do not provide enough information to use the term “fingerprint”. The term fingerprint is reserved for technologies that can uniquely identify a sample with a high enough fidelity for the law.

A shared micro-chemotype, while valuable information, is no guarantee of identical manufacturing origin. Likewise, many of the terpenes that make up the micro-chemotype are both highly volatile with differential vapor pressures suggesting terpene content is highly subject to evaporative or oxidative decay. DNA is more stable in this regard, but highly purified extracts may lack DNA. Such isolated compounds are usually less relevant for DNA characterization as the complexity of the medicine has been greatly purified and simplified. For this reason, DNA is the chosen tracking tool for many nutraceutical manufacturers like GNC⁹.

Sativa vs Indica

After four thorough peer-reviewed manuscripts exploring the Sativa or Indica classification system, the overwhelming consensus is that this nomenclature is meaningless and should be medically ignored.

Chemotyping studies have reinforced this observation^{10, 11 12} and the Sativa or Indica classification is misleading patients to use the wrong medicine. For this reason the Veterans For Cannabis (VFC) has been sequencing and chemotyping every strain they produce and publishing them on the Bitcoin blockchain with the StrainSEEK service. This allows VFC to determine if two strains with the same name in different states are actually identical.

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Why StrainSEEK?

Medicinal Genomics was the first company to sequence the cannabis genome and has the longest history in cannabis genomics of any entity. We are also the only company using blockchains to transparently publish the data in immutable ledgers.

It's Bigger and Better

The StrainSEEK assay covers 3.2 million bases, which is 12 times more sequence data than any other test on the market. Within that 3.2Mbs of data, we have included 24 Cannabinoid and Terpenoid genes to ensure the sequencing is targeted to the genes most selected for breeding. We also included SNPs derived from Sawler, Lynch, Kannapedia, and Phyllos. This Rosetta stone panel enables the most comprehensive assessment of whether a strain is novel or not. We can triangulate strains from everything that is public as of 2017.

It's Legal

We consulted three different law firms on the legality of shipping purified cannabis DNA in the mail and cannabis stalk in the mail. All firms agreed on cannabis legal status for research purposes. DNA is legal to ship in the mail. All tissues must be mature or sterilized with Isopropanol before shipment. This removes cannabinoids and terpenes and makes the tissue non-viable or 'mature'. This material is then exempt of the CSA according to Hemp Industry Associations versus the DEA. Daniel Short from Harris and Bricken recited the following:

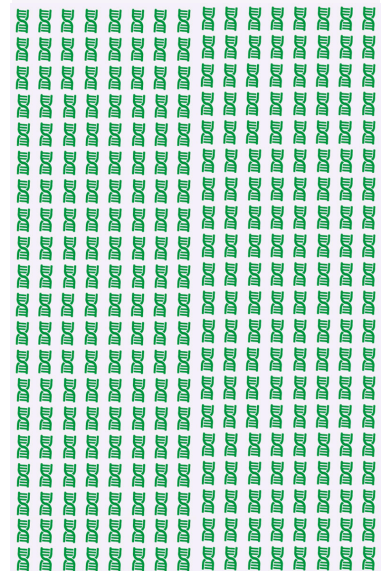
"We cannot formulate a theory that makes "marijuana" legal to possess even for research purposes without obtaining a research license from the DEA. That means the leaf of the plant will remain illegal under federal law regardless of the presence of trichomes or cannabinoids or the stage in the growth cycle. Exempted portions, on the other hand, can be researched legally with the additional caveat that they are not intended for human consumption, which should not be an issue for your research purpose.

There are three portions of the plant [Medicinal Genomics] can research legally: mature stalks, oil or cake made from seeds, and Sterilized seeds."

We have devised methods to obtain isolated DNA from Isopropanol sterilized stalks to remain compliant with the CSA. Other laboratories offer whatman paper smears as a method to deliver Cannabis DNA. We have been advised against this practice.

"Our analysis shows that pressing leaves into paper or accepting the cotyledons is not legal under the CSA. Your competitors may have simply accepted the legal risk, perhaps because federal prosecution over the possession of a small amount of marijuana is extremely unlikely. However, we have looked at this issue many times and through many lenses and have found no loophole allowing for the legal possession of marijuana."

StrainSEEK ASSAY



OTHER ASSAYS



 = 10,000 bases



How Does the StrainSEEK Process Work?

Medicinal Genomics provides stem kits to customers who order the StrainSEEK service from the webstore. The stem kit includes items and instructions for the Isopropanol washing required to insure the stems are clean of cannabinoids and non-viable. These can be shipped in international mail.

When samples arrive at the Medicinal Genomics lab, they are given an RSP number so it can be tracked throughout the sequencing process. Once a strain is sequenced, it is compared to hundreds of other strains in our database and results are published to Kannapedia.net, a public website. Results include the following

- Genetic distance tables that list strains that are most similar and least similar to the sample
- Phylogenetic tree that shows the sample compared to all other strains
- A visualization showing how novel the sample is compared to our database
- Blockchain Hash and Transaction ID
- Fastq and VCF files
- Public QR-Code that references the newly generated web site.
- Optional micro-chemotype table.

It is important to know that not all the sample's genetic data exists in the blockchain due to size limitations of current blockchains. Instead, we use a secure hash algorithm (SHA256) to generate a unique 64-character hash that is based on the content of the sample's VCF file. No other input file in the world can create that same hash, which makes its submission to the blockchain an irrefutable digital notarization for the time of creation for that strain.

Customers are encouraged to download their Fastq and VCF files as a good data backup policy.

Costs

Most cannabis plants are cloned leading to tremendous efficiencies in DNA sequencing. A mother plant can be cloned into thousands of plants and the sequencing need only be performed on the mother. Thus a \$500 sequencing test performed on the mother can provide DNA barcodes for under 50 cents per cloned offspring of the mother. Additional sampling can be performed to spot check the descendant clones as deemed necessary but sequencing every clone would be superfluous.

Step 1: Order Online



Step 2: Collect Stem Sample & Complete Form



Step 3: Send Sample & Form Medicinal Genomics





Conclusions

A blockchain-based genetic catalog of all cannabis in a given market provides transparency to an opaque world of underground names and folklore medicine. We have the unique ability in time to build the most comprehensive cannabis tracking system in the world that will bring patient safety, manufacturer transparency and regulatory comfort. Such a system delivers emergent incentives against diversion and counterfeiting as Blockchain linked mobile phone applications could instantly verify legitimate material with QR code links to Kannapedia.net.

There are lessons we can learn from the reversal of prohibition of alcohol. There is a reason we have \$5 and \$500 bottles of wine on sale in many stores. Consumers believe the labeling system. Yet dispensaries in 2017 rarely have a 2X spread on the price of cannabis for sale. This is a direct result of consumers not trusting the supply chain. If the veracity of high-end products can not be verified, the market for high-end products will never emerge. Manufacturers, consumers, and regulators all win with a blockchained cannabis genetic registry.

References

1. Brunner G. The Bitcoin network outperforms the top 500 supercomputers combined. Extreme Tech. 2013;May 13.
2. Morris DZ. Hackers Cripple Leading Marijuana Sales System. 2017 (Jan 15).
3. Li D, Wang P, Luo Y, Zhao M, Chen F. Health benefits of anthocyanins and molecular mechanisms: Update from recent decade. Critical reviews in food science and nutrition. 2017 May 24;57(8):1729-41. PubMed PMID: 26192537.
4. ElSohly MA, Radwan MM, Gul W, Chandra S, Galal A. Phytochemistry of Cannabis sativa L. Progress in the chemistry of organic natural products. 2017;103:1-36. PubMed PMID: 28120229.
5. Weiblen GD, Wenger JP, Craft KJ, ElSohly MA, Mehmedic Z, Treiber EL, et al. Gene duplication and divergence affecting drug content in Cannabis sativa. New Phytol. 2015 Jul 17. PubMed PMID: 26189495.
6. de Meijer EP, Bagatta M, Carboni A, Crucitti P, Moliterni VM, Ranalli P, et al. The inheritance of chemical phenotype in Cannabis sativa L. Genetics. 2003 Jan;163(1):335-46. PubMed PMID: 12586720. Pubmed Central PMCID: 1462421.
7. Onofri C, de Meijer EP, Mandolino G. Sequence heterogeneity of cannabidiolic- and tetrahydrocannabinolic acid-synthase in Cannabis sativa L. and its relationship with chemical phenotype. Phytochemistry. 2015 Aug;116:57-68. PubMed PMID: 25865737.
8. McKernan KJ, Helbert Y, Tadigotla V, McLaughlin S, Spangler J, Zhang L, et al. Single molecule sequencing of THCA synthase reveals copy number variation in modern drug-type Cannabis sativa L. bioRxiv. 2015.
9. Holliman K. GNC Agrees to Use DNA Barcode Testing. Food Quality and Safety. 2015.
10. Sawler J, Stout JM, Gardner KM, Hudson D, Vidmar J, Butler L, et al. The Genetic Structure of Marijuana and Hemp. PloS one. 2015;10(8):e0133292. PubMed PMID: 26308334. Pubmed Central PMCID: 4550350.
11. Lynch RC, Vergara D, Tittes S, White K, Schwartz CJ, Gibbs MJ, et al. Genomic and Chemical Diversity in Cannabis. bioRxiv. 2015.
12. Elzinga. Cannabinoids and Terpenes as Chemotaxonomic Markers in Cannabis. Natural Products Chemistry & Research. 2015;3(4).