

Cannabinoids and Health

Module 1

Lecture 3: What is cannabis?

Intro to topic via a discussion

- Based on your observations, what are the acute effects of cannabis?
- Where do those effects come from? What explains differences in those effects across people?

The Cannabis Plant

- Cannabis has been under cultivation by humans for millennia (~8000 years+)
- By extension, this means under human selection
- Family is Cannabaceae – Cannabis and Humulus (hops) are relatives in this extended family!
- Some debate about subspecies of cannabis – based on taxonomic and morphological differences
- While academics debate fine details: two subspecies broadly recognized (Sativa and Indica) with some recognition for third (Ruderalis)



Hops

Cannabis

Subspecies

C. sativa ssp. *sativa*

Fiber, oil, food

Medical:Diverse compounds

High biomass

C. sativa ssp. *indica*

Medical:High THC

High yield per height

C. sativa ssp. *ruderalis*

Early flowering, small size

Hardiness

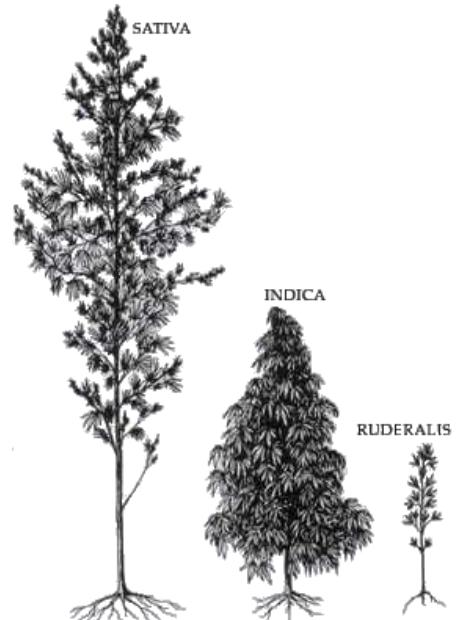


Image: <https://azarius.net/encyclopedia/85/cannabis-types-sativa-indica-ruderalis/>

Correct(ed) Vernacular Nomenclature

INDICA (FORMERLY "SATIVA")



ORIGINAL PROVENANCE: India

MORPHOLOGY: Relatively tall (ca. ≥1.5 m), laxly branched, with narrowly lanceolate leaflets, and relatively sparse flowering tops.

PHYSIOLOGY: Flowering time (seed germination to initiation of reproduction structures under natural conditions) long, 9-14 weeks; no frost tolerance, moderate resin production.

CHEMISTRY: THC much greater than CBD; uniquely prominent terpenoids: sabinene, α-terpinolene, trans-β-ocimene, trans-β-farnesene, imparting a flowery fragrance.

PSYCHOACTIVITY: "Stimulating."

MEDICAL INDICATIONS: Lethargic depression, nausea, appetite stimulation, migraine headaches, and chronic pain. Relative contraindications: insomnia, anxiety, and schizophrenia.

AFGHANICA (FORMERLY "INDICA")



Central Asia (Afghanistan, Turkestan, Pakistan)

MORPHOLOGY: Relatively short (ca. 0.6-1.5 m), densely branched, with broad leaflets often oblanceolate, and dense flowering tops.

PHYSIOLOGY: Flowering time short, 7-9 weeks; frost tolerance, high resin production, susceptible to mold.

CHEMISTRY: Cannabinoid profile variable (THC greater than or roughly equal to CBD); uniquely prominent terpenoids: camphene, β-myrcene, guaiol, β- and γ-eudesmol, imparting an acrid fragrance.

PSYCHOACTIVITY: "Sedating."

MEDICAL INDICATIONS: Insomnia, anxiety, chronic pain, joint stiffness and inflammation, muscle spasms, tremors (from multiple sclerosis and Parkinson's disease), and epilepsy. Relative contraindications: lethargic depression, somnolence, and schizophrenia.

SATIVA (FORMERLY "RUDERALIS")



Usually feral or wild *C. sativa* from Europe, but sometimes of Asian provenance.

Variable, depending on provenance.

Flowering time relatively short but variable, sometimes autoflowering; moderate frost tolerance, relatively low resin production.

CBD>THC; prominent terpenoids: β-caryophyllene, myrcene, imparting a flowery fragrance.

Usually lacking.

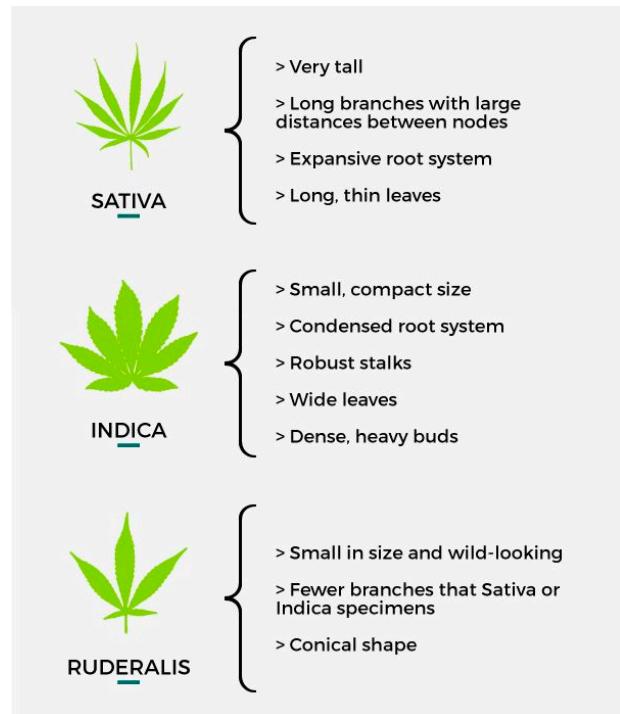
Chronic pain, joint stiffness and inflammation, epilepsy. Relative contraindications: allergy to cannabis.

REVISED VERNACULAR NOMENCLATURE was proposed by John McPartland at the 2014 meeting of the International Cannabinoid Research Society. His paper, co-authored by Geoffrey Guy, used "DNA barcodes" to determine whether or not *Cannabis indica* and *Cannabis sativa* are separate species. The answer was not. *C. indica* and

C. sativa are subspecies —separate varieties of one *Cannabis* species. McPartland traced the confusion that prevails today among plant breeders and the pot-loving masses to the 1970s, when a *C. afghanica* plant collected by botanist Richard Evans Schultes was incorrectly identified as *C. indica*.

Research on The Cannabis Plant

- How do scientists study the plant?
- Morphology (shape of the leaves, etc).
- Chemical (e.g., chemovars)
- Underlying genetic architecture
- Why is this important in terms of the medical effects?



- Plant structure illustrated on right
- Flowers of female plants covered with sticky, resinous trichomes
- Trichomes contain most of the 104+ cannabinoids, terpenes, etc.

Parts of the Cannabis Plant

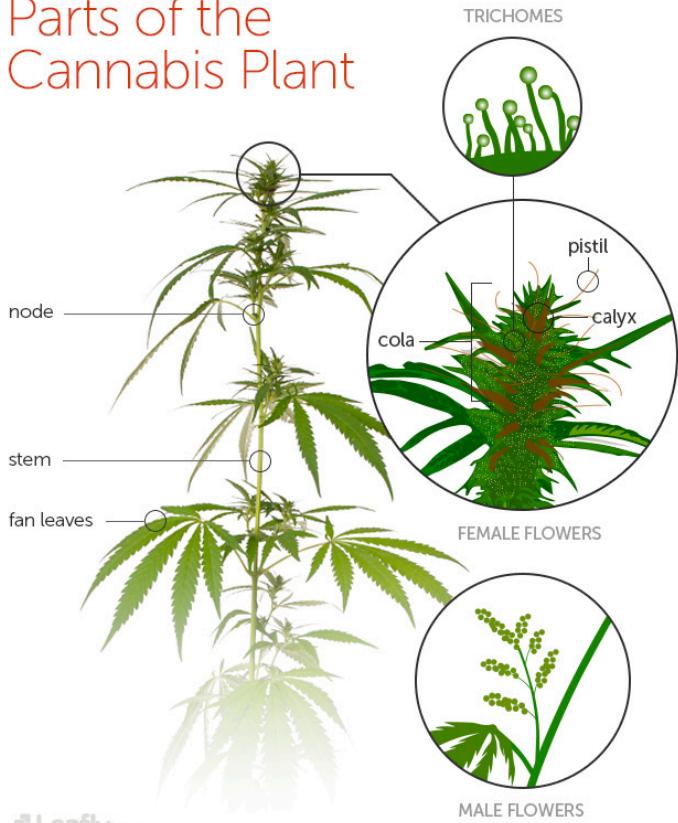


Image: <https://www.leafly.com/news/cannabis-101/cannabis-anatomy-the-parts-of-the-plant>

THC and CBD

- Trichomes and cannabinoids found throughout plant
- Most concentrated in buds/flowers
- Two most studied cannabinoids are THC and CBD



Chemistry

- Cannabigerolic Acid (CBG) is the precursor for THC and CBD
- Synthases convert CBG to THCa and CBDA
- Decarboxylation (e.g., through heat) converts THCa to THC and CBDA to CBD
- Oxidation also turns THC to CBN

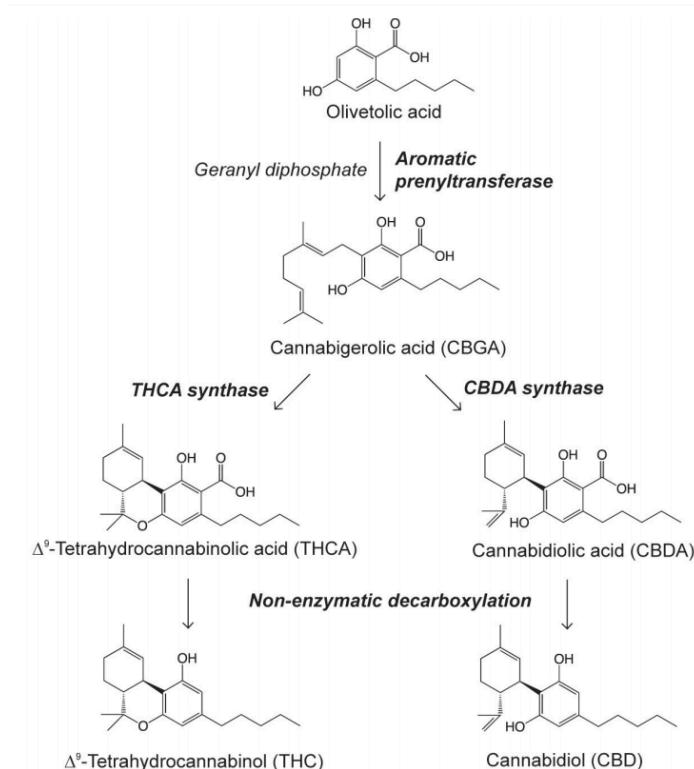
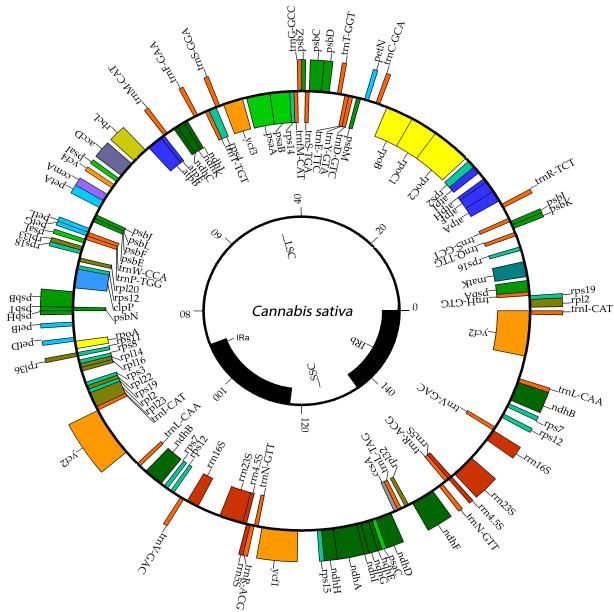


FIGURE 2-1 Synthetic pathway of the main cannabinoids, Δ^9 -THC and CBD, from the common precursor, olivetol.

Cutting Edge Genetic Research (by Nolan Kane and others)

- Over 1000 genomes analyzed
 - Diverse
 - Hemp, landrace, wild, feral, modern
 - Aligned to best current genome



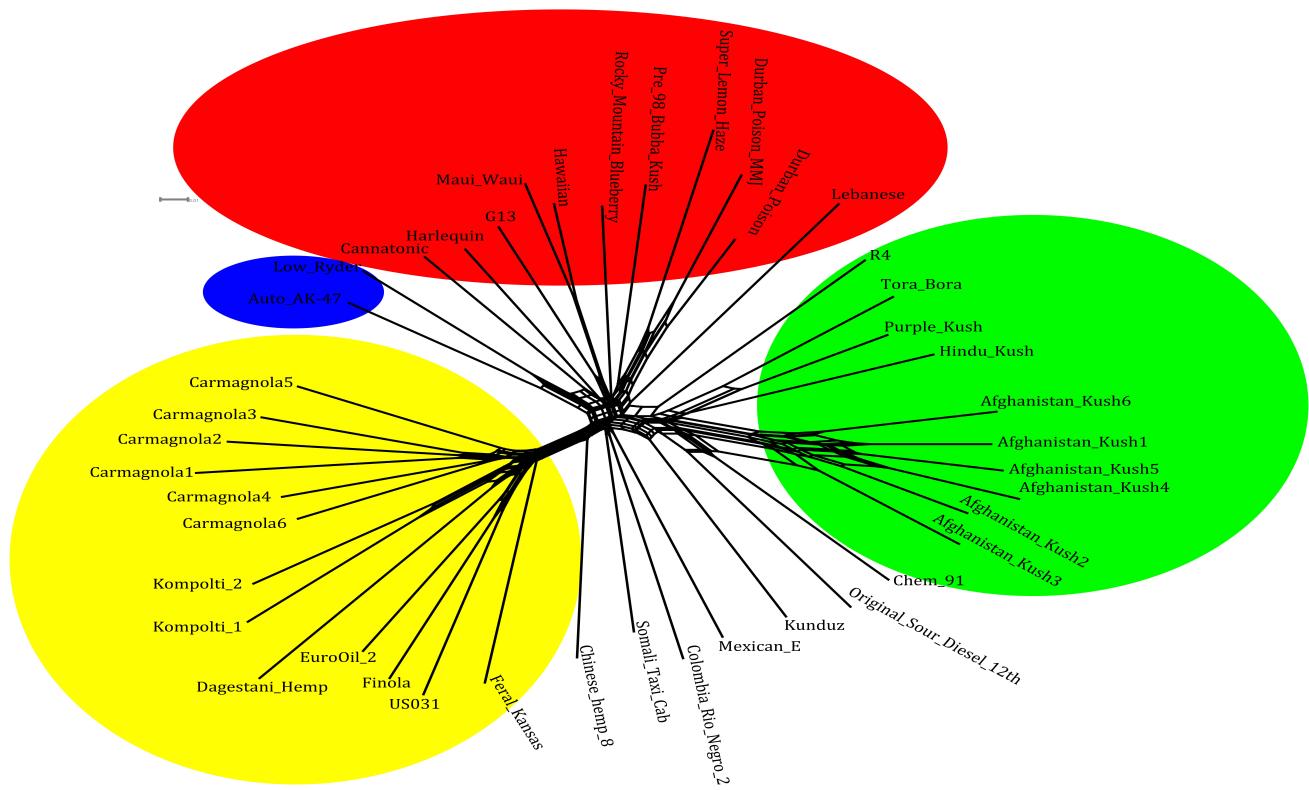
Genomic and Chemical Diversity in *Cannabis*

Ryan C. Lynch, Daniela Vergara, Silas Tittes, Kristin White, C. J. Schwartz,
Matthew J. Gibbs, Travis C. Ruthenburg, Kymron deCesare, Donald P. Land &
Nolan C. Kane

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(2016) Genomic and Chemical Diversity in *Cannabis*, Critical Reviews in Plant Sciences, 35:5-6,
349-363, DOI: [10.1080/07352689.2016.1265363](https://doi.org/10.1080/07352689.2016.1265363)

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Phylogenetic Neighbor Network

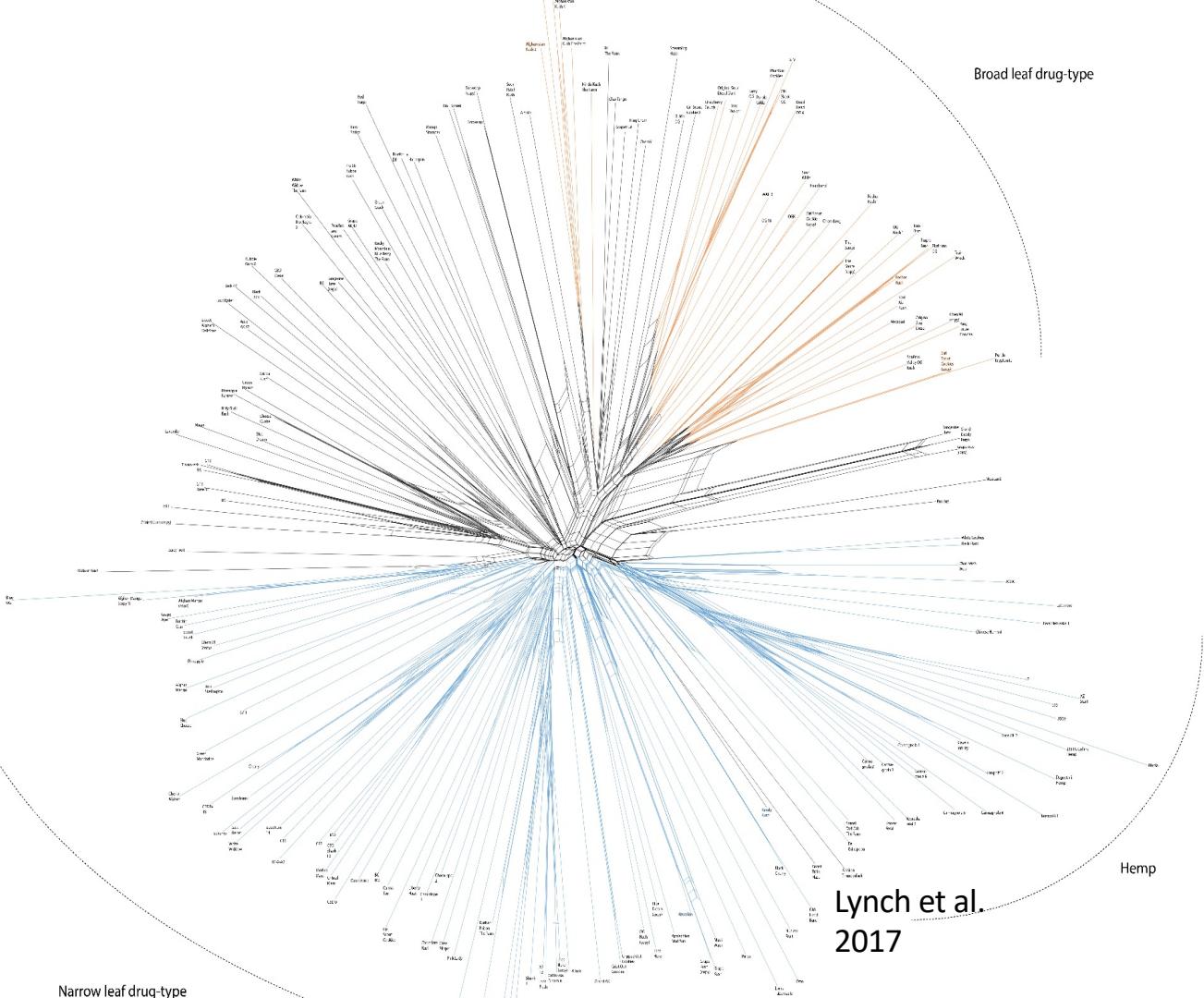


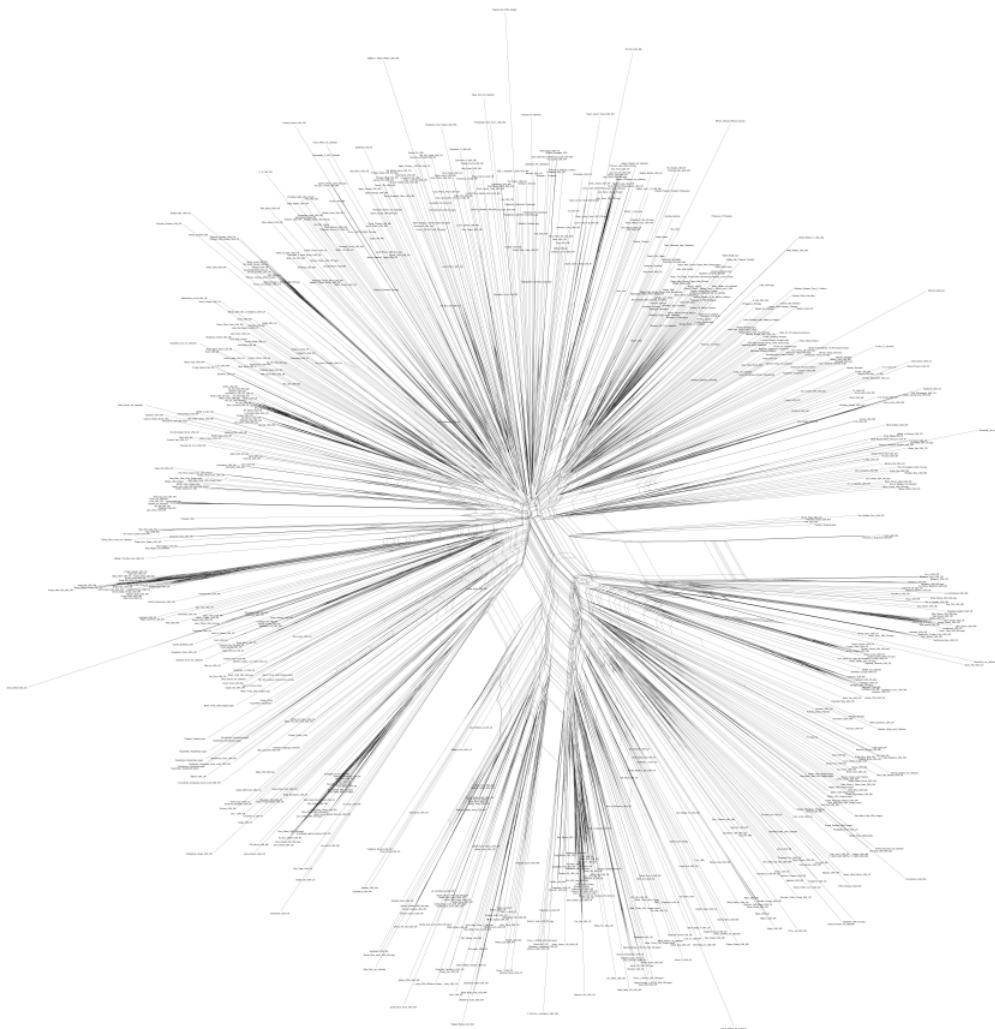
Broad leaf drug-type

Lynch et al.
2017

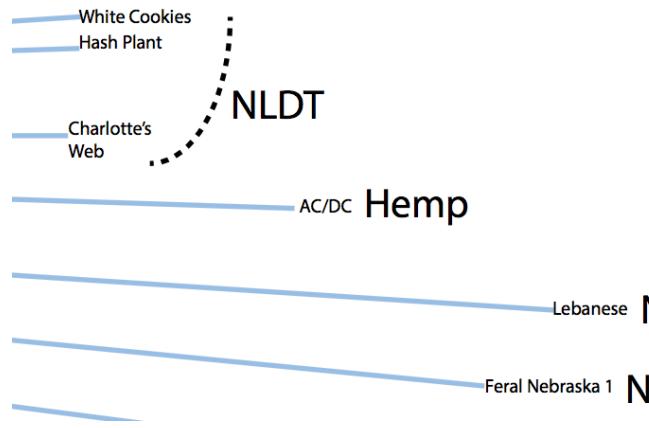
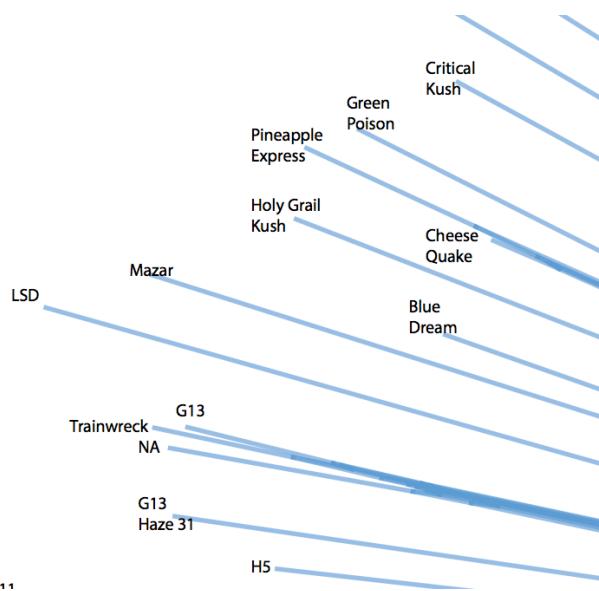
Hemp

Narrow leaf drug-type

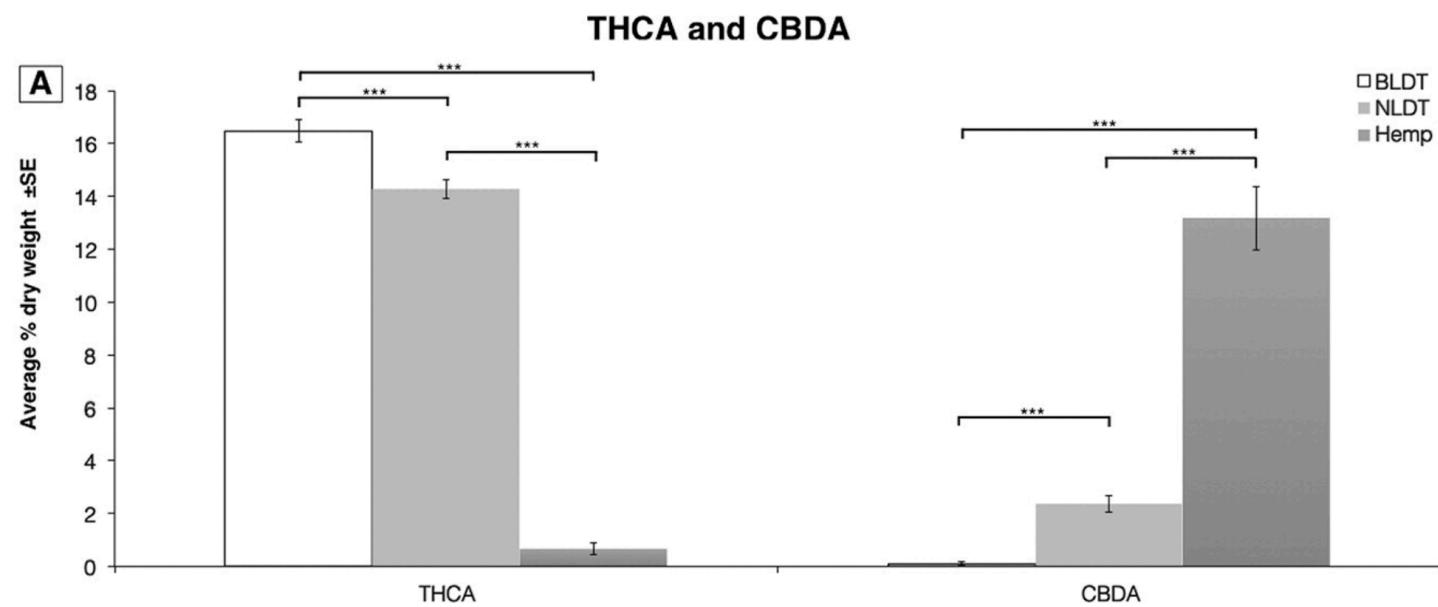




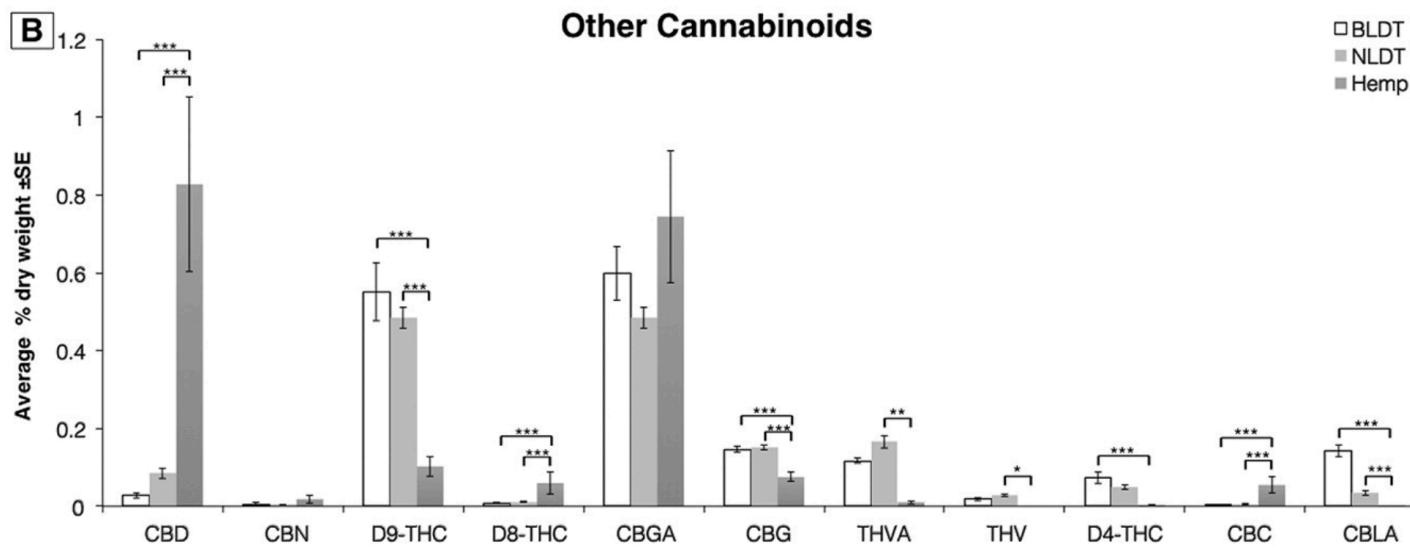
A close up...



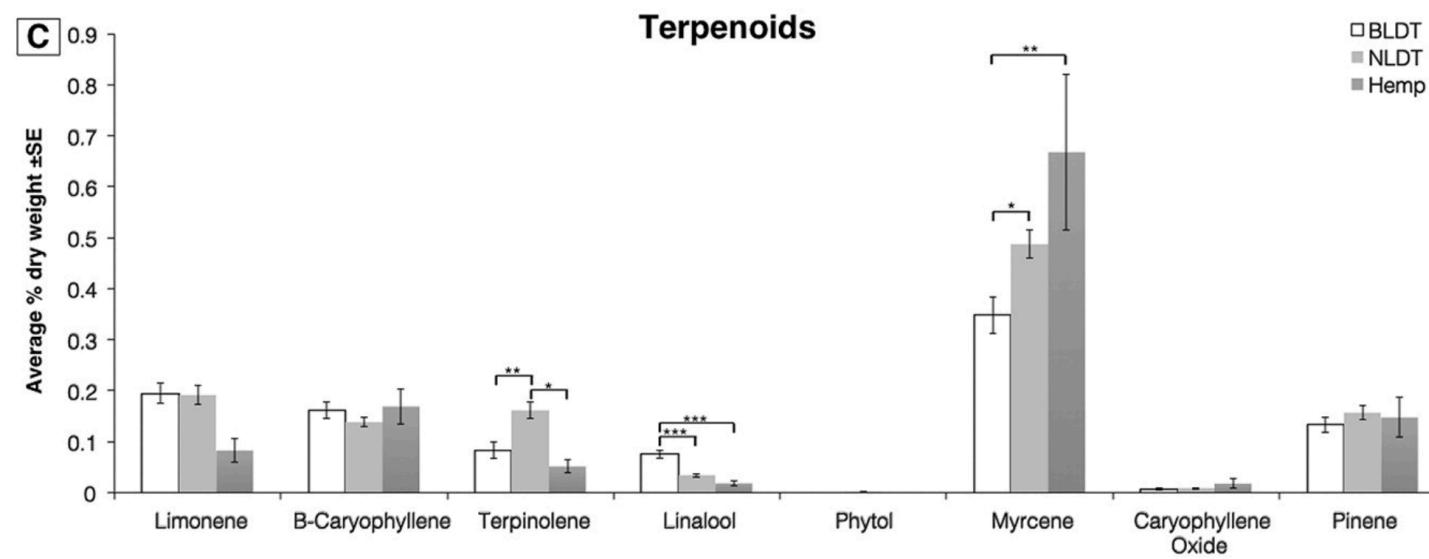
THC and CBD Differences



Differences: Other Cannabinoids



Differences in Terpenes



Genetic variation within *Cannabis*

- There are at least 3 major lineages
- These lineages differ genetically, morphologically, ecologically, and chemically
- Anecdotally, people report different effects of different strains
- The reported differences among lineages may be due to complex interactions among many cannabinoids and terpenes

Chemovars

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THE HEALTH EFFECTS OF CANNABIS AND CANNABINOIDS

TABLE 2-1 Cannabis Phenotypes

Chemotype	Δ^9 -THC	CBD	CBD: Δ^9 -THC ratio
THC-type	0.5–15%	0.01–0.16%	<0.02
Hybrid	0.5–5%	0.9–7.3%	0.6–4
CBD-type	0.05–0.7%	1.0–13.6%	>5

NOTE: THCA-predominant strains can yield more than 25 percent Δ^9 -THC; specifically selected CBDA clones can yield up to 20 percent CBD.

SOURCE: Modified from Galal et al., 2009.

Cannabis for federal studies

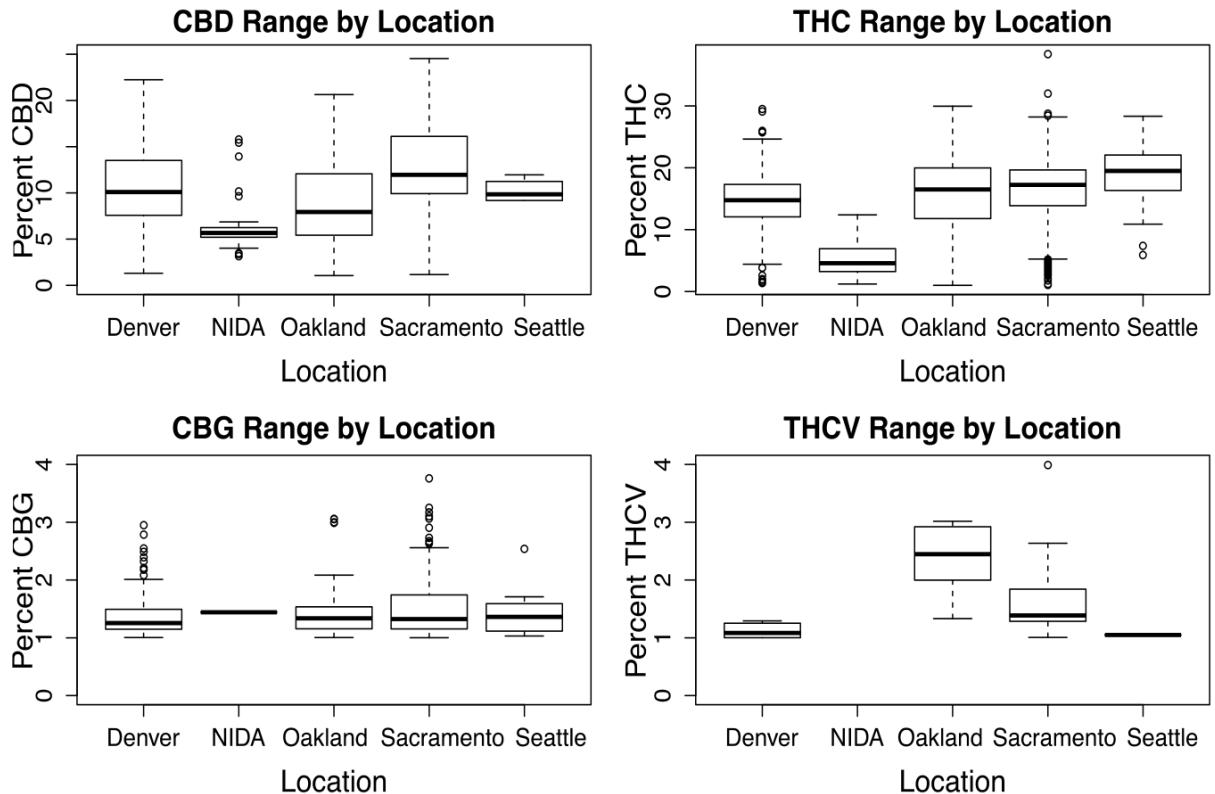
- For over 50 years the sole source of *Cannabis* for federal studies has been the University of Mississippi
- Discussion: Do you think the cannabis grown by the federal government in MS reflects the cannabis in the real world? Why or why not? How might it be different? How might that impact our scientific knowledge?

Article | **OPEN** | Published: 19 April 2017

Compromised External Validity: Federally Produced Cannabis Does Not Reflect Legal Markets

Daniela Vergara , L. Cinnamon Bidwell, Reggie Gaudino, Anthony Torres, Gary Du, Travis C. Ruthenburg, Kymron deCesare, Donald P. Land, Kent E. Hutchison & Nolan C. Kane 

Scientific Reports **7**, Article number: 46528 (2017) | [Download Citation ↓](#)



What is different about NIDA?

- NIDA's varieties contain lower THC levels
- NIDA's varieties also have lower CBD levels
- NIDA reports no measurable THCV or other 'minor' cannabinoids or terpenes
- This is changing for the better as NIDA has worked hard to catch up with state-legalized markets
- NIDA is now providing products that more closely resemble cannabis in legal markets
- But it is hard to keep up!!!

Summary

- There are at least 3 major lineages of *Cannabis*, including hemp, broad leaf drug types, and narrow leaf drug types
- These lineages differ in cannabinoids and terpenes, which may partially explain reported differences in effects