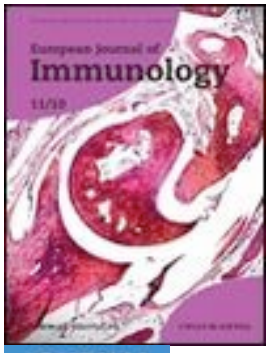
This file contains a spectrum of research articles and field notes on cannabis and immunity.

The situation regarding cannabis and immunity is complex. THC and other cannabinoids target natural cannabinoid receptors, both in the brain and immune system, just as our endocannabinoids such as anandamide do.

The effect of cannabis on the immune system is immunomodulatory - that is it alters the internal balance of immunity to quieten it down. Some findings suggest a significant reduction in killer cells, but there is little evidence for actual impaired immunity, even in immune suppressed individuals, such as HIV patients.

So although there may be some concerns that cannabis might reduce immune vigilance in infection and possibly cancer, it could prove beneficial in auto-immune conditions.

New Study Reveals How Cannabis Suppresses Immune Functions



European Journal of Immunology
ISSN: 0014-2980

November 25, 2010

New Study Reveals How Cannabis Suppresses Immune Functions

An international team of immunologists studying the effects of cannabis have discovered how smoking marijuana can trigger a suppression of the body's immune functions. The research, published in the European Journal of Immunology, reveals why cannabis users are more susceptible to certain types of cancers and infections.

The team, led by Dr Prakash Nagarkatti from the University of South Carolina, focused their research on cannabinoids, a group of compounds found inside the cannabis plant, including THC (delta-9 tetahydrocannabinol) which is already used for medical purposes such as pain relief.

"Cannabis is one of the most widely used drugs of abuse worldwide and it is already believed to suppress immune functions making the user more susceptible to infections and some types of cancer," said Dr Nagarkatti. "We believe the key to this suppression is a unique type of

immune cell, which has only recently been identified by immunologists, called myeloid-derived suppressor cells, MDSCs."

While most immune cells fight against infections and cancers to protect the host, MDSCs actively suppress the immune system. The presence of these cells is known to increase in cancer patients and it is believed that MDSCs may suppress the immune system against cancer therapy, actually promoting cancer growth.

Dr Nagarkatti's team demonstrated that cannabinoids can trigger a massive number of MDSCs through activation of cannabinoid receptors. This research reveals, for the first time, that marijuana cannabinoids may suppress the immune system by activating these unique cells.

"These results raise interesting questions on whether increased susceptibility to certain types of cancers or infections caused from smoking marijuana results from induction of MDSCs," said Nagarkatti. "MDSCs seem to be unique and important cells that may be triggered by inappropriate production of certain growth factors by cancer cells or other chemical agents such as cannabinoids, which lead to a suppression of the immune system's response."

In a related study, also published in the European journal of Immunology, Dr Christian Vosshenrich from the Institut Pasteur in Paris, reveals that when cancer cells grow they produce a molecule called interleukin-1 β (IL-1β), which also triggers MDSCs. This study identifies how MDSCs produced during cancer growth also weaken the ability of immune cells to kill cancer cells.

"Marijuana cannabinoids present us with a double edged sword," concluded Dr Nagarkatti. "On one hand, due to their immunosuppressive nature, they can cause increased susceptibility to cancer and infections. However, further research of these compounds could provide opportunities to treat a large number of clinical disorders where suppressing the immune response is actually beneficial."

1: Mini Rev Med Chem. 2005 Jul;5(7):671-5.Click here to read Links

The role of cannabinoid system on immune modulation: therapeutic implications on CNS inflammation.

Correa F, Mestre L, Molina-Holgado E, Arévalo-Martín A, Docagne F, Romero E, Molina-Holgado F, Borrell J, Guaza C.

Neural Plasticity Unit, Neuroimmunology Group, Instituto Cajal, Consejo Superior de Investigaciones Científicas, Madrid, Spain.

There is a growing amount of evidence suggesting that cannabinoids may be neuroprotective in CNS inflammatory conditions. Advances in the understanding of the physiology and pharmacology of the cannabinoid system have increased the interest of cannabinoids as potential therapeutic targets. Cannabinoid receptors and their endogenous ligands, the endocannabinoids, have been detected in cells of the immune system, as well as in brain glial cells. In the present review it is summarized the effects of cannabinoids on immune reactivity and on the regulation of neuroinflammatory processes associated with brain disorders with special attention to chronic inflammatory demyelinating diseases such as multiple sclerosis.

1: J Neuroimmunol. 2005 Sep;166(1-2):3-18.Click here to read Links
Cannabinoids and the immune system: potential for the treatment of inflammatory diseases?
Croxford JL, Yamamura T.

Department of Immunology, National Institute of Neuroscience, NCNP, 4-1-1 Ogawahigashi, Kodaira, Tokyo 187-8502, Japan. croxford@ncnp.go.jp

Since the discovery of the cannabinoid receptors and their endogenous ligands, significant advances have been made in studying the physiological function of the endocannabinoid system. The presence of cannabinoid receptors on cells of the immune system and anecdotal and historical evidence suggesting that cannabis use has potent immuno-modulatory effects, has led to research directed at understanding the function and role of these receptors within the context of immunological cellular function. Studies from chronic cannabis smokers have provided much of the evidence for immunomodulatory effects of cannabis in humans, and animal and in vitro studies of immune cells such as T cells and macrophages have also provided important evidence. Cannabinoids can modulate both the function and secretion of cytokines from immune cells. Therefore, cannabinoids may be considered for treatment of inflammatory disease. This review article will highlight recent research on cannabinoids and how they interact with the immune system and also their potential use as therapeutic agents for a number of inflammatory disorders.

: JAMA. 2003 Aug 13;290(6):754; author reply 755.Click here to read
Cannabinoids and immune function.
Killestein J, Uitdehaag BM, Polman CH.

1: JAMA. 2003 Apr 16;289(15):1929-31.Click here to read Links

Comment in:
JAMA. 2003 Aug 13;290(6):754; author reply 755.

Modulation of the immune system in cannabis users.
Pacifici R, Zuccaro P, Pichini S, Roset PN, Poudevida S, Farré M, Segura J, De la Torre R.

JAMA Vol. 289 No. 15, April 16, 2003 TABLE OF CONTENTS

Modulation of the Immune System in Cannabis Users

To the Editor: In vitro studies and experiments in animal models have found that cannabinoids modulate immune cell function.1 However, investigations of immune effects in human subjects are scarce and contradictory. Gene expression of cannabinoid receptors in peripheral blood mononuclear cells may be altered among marijuana users.2 Experimental data in healthy persons have found abnormalities in T lymphocyte and natural killer (NK) cell function, but have not confirmed that these alterations might affect susceptibility to infections.3 We sought to investigate cell-mediated immune response and cytokine release in cannabis

users.

Methods. Participants were recruited by word of mouth and gave written consent to participate in the study, which was approved by our institutional ethical committee and conducted in accordance with the Declaration of Helsinki. Volunteers were deemed healthy after a full medical history and examination. They were then interviewed about their recent use of illicit drugs, and their statements were confirmed by urine testing. A psychiatric screening excluded drug abuse or dependence (except for cannabis or nicotine) or psychiatric disorders according to criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.

A blood sample was obtained between the hours of 8 and 11 AM to determine blood cell count and differential, lymphocyte immunophenotyping, lymphocyte proliferative response to mitogenic stimulation (stimulation index with phytohemoagglutinine [SI-PHA] or concanavaline A [SI-ConA]), and levels of interleukin 2 (IL-2), interleukin 10 (IL-10), and transforming growth factor {beta}-1 (TGF{beta}1), as described previously.4 Comparisons between cannabis exposure categories were performed using {chi}2 tests or analysis of variance. Multivariate linear regression models were fitted for each immune parameter to analyze the effects of cannabis consumption after adjusting for sex, as well as consumption of coffee, tobacco, and alcohol.

Results. According to total cannabis consumption and frequency of use during the previous 6 months, participants were classified as controls (n = 32), occasional users (eventual to monthly use, n = 13) and regular users (weekly to daily use, n = 16). Sex, tobacco smoking, and alcohol consumption were unequally distributed between groups (Table 1).

Table. Group Characteristics and Immune Parameters in Controls and Cannabis

Characteristic/Parameter	Controls (n = 32)	Cannabis Co: Occasio (n =
Age, mean (SD), y	22 (3)	21
Sex distribution, No (%)		
Male	23 (72)	12
Female	9 (28)	1
Coffee consumption, No (%)		
Daily	15 (47)	8
Occasionally/none	17 (53)	5
Tobacco smoking, No (%)		
Daily	4 (13)	2
Weekly	3 (9)	3
Occasionally/none	25 (78)	8
Alcohol consumption, No (%)		
Daily	0	
Weekly	23 (72)	11
Occasionally/none	9 (28)	2
Immune parameters, mean (SD)		
Total lymphocytes, cells/μL	1950 (152)	1901
CD4 T cells, cells/μL	933 (105)	929
CD8 T cells, cells/μL	548 (98)	574
CD19 B cells, cells/μL	182 (61)	142
NK cells, cells/μL	203 (82)	145
SI-PHA, %	96 (15)	97
SI-ConA, %	75 (17)	75
IL-2, U/mL	10.6 (3.8)	8.6
IL-10, pg/mL	903 (191)	1284
TGFβ1, pg/mL	660 (172)	1450

Abbreviations: IL-2, interleukin 2; IL-10, interleukin 10; SI-ConA, mitogenic stimulation index by conca
transforming growth factor β-1.
*From χ^2 test or analysis of variance.
†Significant difference ($P<.05$) between controls and regular users, by analysis of variance post ho
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Table. Group Characteristics and Immune Parameters in Controls and Cannabis Users

Cannabis use was associated with a decrease in NK counts, lymphocyte

proliferative response by SI-PHA and SI-ConA, and levels of IL-2, and an increase in levels of IL-10 and TGF{beta}1. No differences were found in counts of total lymphocytes or CD4, CD8, and CD19 cells (TABLE). The significant effect of cannabis consumption on immune measures persisted after multivariate analysis controlling for the possible confounding effects of sex and use of coffee, tobacco, and alcohol. A significant dose-response relationship was found between cannabis exposure (total life consumption, as the log-transformed number of cannabis "joints") and the decrease in counts of total lymphocytes, CD4 or NK cells, and IL-2 levels, or the increase in IL-10 levels.

Comment. Cannabis use was associated with a decrease in levels of IL-2, a TH1-type cytokine related to cell-mediated immunity, and an increase in levels of IL-10, a TH2-type cytokine related to humoral immunity. The decrease of proinflammatory (IL-2) cytokines and the augment of anti-inflammatory (IL-10 and TGF{beta}1) cytokines was associated with a marked reduction in lymphocyte functionality, and a decrease in the number of NK cells. The suppression of immediate and innate responses of the immune system together with the disruption of TH1/TH2 balance might increase the susceptibility and promote the progression of infectious diseases and tumors, although the clinical relevance of these findings has not been clearly demonstrated in humans.3, 5 It also has been suggested that immunomodulatory effects of cannabinoids on inflammatory and autoimmune disorders could lead to new therapeutic interventions.6

Modulation of the Immune System in Cannabis Users

To the Editor: In vitro studies and experiments in animal models have found that cannabinoids modulate immune cell function.[1] However, investigations of immune effects in human subjects are scarce and contradictory. Gene expression of cannabinoid receptors in peripheral blood mononuclear cells may be altered among marijuana users.[2] Experimental data in healthy persons have found abnormalities in T lymphocyte and natural killer (NK) cell function, but have not confirmed that these alterations might affect susceptibility to infections.[3] We sought to investigate cell-mediated immune response and cytokine release in cannabis users.

Methods. Participants were recruited by word of mouth and gave written consent to participate in the study, which was approved by our institutional ethical committee and conducted in accordance with the Declaration of Helsinki. Volunteers were deemed healthy after a full medical history and examination. They were then interviewed about their recent use of illicit drugs, and their statements were confirmed by urine testing. A psychiatric screening excluded drug abuse or dependence (except for cannabis or nicotine) or psychiatric disorders according to criteria of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*.

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(TGFβ1), as described previously.[4] Comparisons between cannabis exposure categories were performed using χ^2 tests or analysis of variance. Multivariate linear regression models were fitted for each immune parameter to analyze the effects of cannabis consumption after adjusting for sex, as well as consumption of coffee, tobacco, and alcohol.

Results. According to total cannabis consumption and frequency of use during the previous 6 months, participants were classified as controls (n = 32), occasional users (eventual to monthly use, n = 13) and regular users (weekly to daily use, n = 16). Sex, tobacco smoking, and alcohol consumption were unequally distributed between groups (Table 1).

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Immune parameters, mean (SD)		
Total lymphocytes, cells/μL	1950 (152)	19
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Abbreviations: IL-2, interleukin 2; IL-10, interleukin 10; SI-ConA, mitogenic stimulation index by co
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Table. Group Characteristics and Immune Parameters in Controls and Cannabis Users

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1. Klein TW, Newton C, Friedman H. Cannabinoids receptors and immunity. *Immunol Today.* 1998;19:373-381. FULL TEXT | WEB OF SCIENCE | PUBMED

2. Nong L, Newton C, Cheng Q, Friedman H, Roth MD, Klein TW. Altered cannabinoid receptor mRNA expression in peripheral blood mononuclear cells from marijuana smokers. *J Neuroimmunol.* 2002;127:169-176. FULL TEXT | PUBMED

3. Kaslow RA, Blackwelder WC, Ostrow DG, et al. No evidence for a role of alcohol or other psychoactive drugs in accelerating immunodeficiency in HIV-1-positive individuals: a report from the Multicenter AIDS Cohort Study. *JAMA.* 1989;261:3424-3429. **FREE** FULL TEXT

4. Pacifici R, Zuccaro P, Hernández-López, et al. Acute effects of 3,4-methylenedioxymethamphetamine alone and in combination with ethanol on the immune system in humans. *J Pharmacol Exp Ther.* 2001;296:207-215. **FREE** FULL TEXT

5. Roth MD, Baldwin GC, Tashkin DP. Effects of delta-9-tetrahydrocannabinol on human immune function and host defense. *Chem Phys Lipids.* 2002;121:229-239. FULL TEXT | WEB OF SCIENCE | PUBMED

6. Zurier RB. Prospects for cannabinoids as anti-inflammatory agents. *J Cell Biochem.* 2003;88:462-466. FULL TEXT | WEB OF SCIENCE | PUBMED

Letters Section Editor: Stephen J. Lurie, MD, PhD, Senior Editor.

JAMA. 2003;289:1929-1931.

How cannabis dampens the immune system

- 03 December 2010
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CANNABIS is a double-edged sword: by dampening the immune system, it provides relief from inflammatory diseases, but this also increase the risk of infections. Now we know how it does this: its active ingredient targets a newly discovered type of cell that lowers the immune response.

Prakash Nagarkatti at the University of South Carolina School of Medicine and colleagues injected the main active ingredient of cannabis, delta-9-tetrahydrocannabinol (THC), into mice. THC activated two types of cannabinoid receptor on immune cells, called CB1 and CB2. Activation of these receptors led to a "massive mobilisation" of myeloid-derived suppressor cells (MDSCs), which play a crucial role in lowering the immune system response back down to normal levels (*European Journal of Immunology*, DOI: 10.1002/eji.201040667).

The discovery offers a possible explanation of why cannabis smokers have a higher risk of getting infections, says Nagarkatti. It may also mean THC could be used when there is a need to suppress the immune system - after an organ transplant, for example.

Myth: Marijuana Use Impairs the Immune System. Marijuana users are at increased risk of infection, including HIV. AIDS patients are particularly vulnerable to marijuana's immunopathic effects because their immune systems are already suppressed.

Fact: There is no evidence that marijuana users are more susceptible to infections than nonusers. Nor is there evidence that marijuana lowers users' resistance to sexually transmitted diseases. Early studies which showed decreased immune function in cells taken from marijuana users have since been disproved. Animals given extremely large doses of THC and exposed to a virus have higher rates of infection. Such studies have little relevance to humans. Even among people with existing immune disorders, such as AIDS, marijuana use appears to be relatively safe. However, the recent finding of an association between tobacco smoking and lung infection in AIDS patients warrants further research into possible harm from marijuana smoking in immune suppressed persons.

- Parents Resource Institute for Drug Education. Marijuana and Cocaine. Atlanta: PRIDE, 1990.

- Preate, Ernest D. Blowing Away the Marijuana Smokescreen. Scranton: Pennsylvania Office of Attorney General, [no date]: 2.
- Spence, W.R. Marijuana: Its Effects and Hazards. Waco: Health Edco, [no date].
- Voth, Eric A. The International Drug Strategy Institute Position Paper on the Medical Applications of Marijuana. Omaha: Drug Watch International, [no date].
- Drug Watch International. By Any Modern Medical Standard, Marijuana is No Medicine. Omaha: Drug Watch International, [no date].

Myth: Marijuana's Active Ingredient, THC, Gets Trapped in Body Fat. Because THC is released from fat cells slowly, psychoactive effects may last for days or weeks following use. THC's long persistence in the body damages organs that are high in fat content, the brain in particular.

Fact: Many active drugs enter the body's fat cells. What is different (but not unique) about THC is that it exits fat cells slowly. As a result, traces of marijuana can be found in the body for days or weeks following ingestion. However, within a few hours of smoking marijuana, the amount of THC in the brain falls below the concentration required for detectable psychoactivity. The fat cells in which THC lingers are not harmed by the drug's presence, nor is the brain or other organs. The most important consequence of marijuana's slow excretion is that it can be detected in blood, urine, and tissue long after it is used, and long after its psychoactivity has ended.

- Committees of Correspondence. Drug Abuse Newsletter 16 (March 1984).
- Mann, Peggy. Marijuana Alert. New York: McGraw-Hill Book Company. 1985. 184.
- Nahas, Gabriel. "When Friends of Patients Ask About Marihuana." Journal of the American Medical Association 233 (1979): 79.
- DuPont, Robert. Getting Tough on Gateway Drugs. Washington, DC: American Psychiatric Press, 1984. 68.
-

• Immune Responses

- Immune responses protect the body from disease through the development of various “defense cells,” such as antibodies, macrophages, and T cells. Research of the immunobiological effects of cannabis is widely contradictory. Biased researchers have often interpreted ambiguous evidence according to preconceived theories.[1] Test-tube studies finding cellular suppression of immune responses have been flawed by their use of extremely high concentrations of cannabinoids, levels impossible to obtain in actual use.[2] The same flaw is found In research cited as proof that cannabinoids impair cellular metabolism.[3] Misinformed persons might consider that AIDS patients are a high-risk group for possible immune complications brought about by the use of medical marijuana, but there is no clinical or epidemiological evidence linking cannabis use to immune suppression.[4] According to cannabis researcher Leo Hollister,

- Clinically, one might assume that sustained impairment of cell-mediated immunity might lead to an increased prevalence of malignancy. No such clinical evidence has been discoved or has any direct epidemiological data incriminated marijuana use with the acquisition of human immunodeficiency virus or the clinical development of AIDS.[5]

- Clinical evidence of immune suppression is somewhat contradictory. For

example, N.E. Kaminsky stated in the *Journal of Neuroimmunology*, "I think that these (cannabinoids) might be useful as a relatively weak immune modulators, perhaps to be used as anti-inflammatory agents or even maybe for asthma." [6] (Asthma is thought to be an autoimmune disease).

- Modern understandings of the endocannabinoid systems within the human body show that cannabinoids are actually building blocks of our immune systems. Dr. Donald Abrams, one of the foremost authorities on cannabis in the treatment of HIV and AIDS reports:

- **"** The CB2 receptor, interestingly, the second cannabinoid receprot, is not found in the brain at all, but is predominantly located in the immune issues, the macrophages which are circulating blood cells that go into tissues and fight infections, and also the spleen." [7]

- Research also indicates that the tolerance factor found in most aspects of cannabis use probably protects the subject from any potential immunological dangers. Immune suppression that may be caused by a large overdose of cannabinoids has shown to be reduced by repeated exposure.[8]

- Several human studies of large cannabis-using populations show no difference in disease susceptibility between cannabis users and nonusers. [9] According to the United Nations World Health Organization in 1997,

- To date there has been no epidemiological evidence of increased rates of disease among heavy cannabis users. Given the duration of large scale cannabis use by young adults in Western societies, the absence of any epidemics of infectious disease makes it unlikely that cannabis smoking produces major impairments in the immune system.[10]

- It is possible that a small percentage of users may develop allergies to cannabinoids with repeated exposure. It is also possible that the rarely documented cases of allergic reactions to smoked cannabis have been caused by other factors such as fungi, mold, toxic insecticides, and/or herbicides. Because of the possibility of exposure to contaminant hazards, AIDS sufferers and patients with other immune deficiencies should not obtain cannabis through illegal non-medical markets.

- Related sections: *Cardiovascular Effects, Contaminants, Smoking Methods, Tolerance, Upper Respiratory Infection.*

-

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- [1] Hollister, "Health aspects of marijuana." *Pharmacological Review*, Vol. 38, No. 1, 1986

- [2] Hollister, "Marijuana and immunity." *Journal of Psychoactive Drugs*, Vol. 24, pp. 159-63, 1992

- [3] *World Health Organization Project on Health, Implications of Cannabis Use*, 1997

- [4] “The health and psychological consequences of cannabis use.” Chapter 6, *National Drug Strategy Monograph No. 25*, Australia
- [5] Hollister, *op. cit.*
- [6] Finn, “Cannabinoid investigations entering the mainstream.” *The Scientist*, Vol. 12, No. 3, pp. 1-8, February 2, 1998
- [7] Abrams. Lecture, Lindesmith Center, San Francisco, May 17, 1999
- [8] Loveless, Harris, and Munson, “Hyporesponsiveness to the immunosuppressant effects of delta-8 tetrahydrocannabinol.” *Journal of Immunopharmacology*, Vol. 3, No. 3-4, pp. 371-383, 1981
- [9] Zimmer and Morgan, *Marijuana Myths: Marijuana Facts*. New York: The Lindesmith Center
- [10] World Health Organization, *op. cit.*

- Vol 40 Issue 12 >

European Journal of Immunology

Highlights

Cannabinoid receptor activation leads to massive mobilization of myeloid-derived suppressor cells with potent immunosuppressive properties

1. Venkatesh L. Hegde,
2. Mitzi Nagarkatti,
3. Prakash S. Nagarkatti

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Cannabis Might Lower Immune Function, Raise Cancer Risk
NOV 25 2010 - EMax health

Researchers from the University of South Carolina say cannabis users may be more prone to infections and cancer from suppression of immune function. The study authors say cannabinoids including THC in marijuana triggers the production of high numbers of myeloid-derived suppressor cells, MDSCs that have just recently been identified by immunologists and found in high levels in cancer patients.

Unlike other immune fighting cells, MDSCs suppress immunity. Dr Prakash Nagarkatti from the University of South Carolina studied compounds in marijuana that are currently used for medicinal purposes and found in the plant.

Immune Suppressing Action of Cannabis Could Prove Beneficial

Though the researchers found cannabis can stimulate large numbers of MDSCs, Dr. Nagarkatti says there may be instances when suppressing immunity could be helpful. He says, "Marijuana cannabinoids present us with a double edged sword. On one hand, due to their immunosuppressive nature, they can cause increased susceptibility to cancer and infections. However, further research of these compounds could provide opportunities to treat a large number of clinical disorders where suppressing the immune response is actually beneficial."

He notes the study raises questions about whether MDSCs actually increase susceptibility to cancer and infection. The presence of the immune suppressing MDSCs if known to increase in cancer patients, increase the chances of infection and promote cancer growth.

In a related study published in the European journal of Immunology, Dr Christian Vosshenrich from the Institut Pasteur in Paris, found that cancer cells also produce interleukin-1 β (IL-1β) that also triggers MDSCs and weaken immunity.

Dr. Narkattie says, "MDSCs seem to be unique and important cells that may be triggered by inappropriate production of certain growth factors by cancer cells or other chemical agents such as cannabinoids, which lead to a suppression of the immune system's response." The findings suggest cannabis users could be more vulnerable to cancer and infection, based on the findings that marijuana compounds stimulate production of the immune suppressing cells.

European Journal of Immunology

Nat Rev Immunol. 2009 Mar;9(3):162-74.

Myeloid-derived suppressor cells as regulators of the immune system.

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Abstract

Myeloid-derived suppressor cells (MDSCs) are a heterogeneous population of cells that expand during cancer, inflammation and infection, and that have a remarkable ability to suppress T-cell responses. These cells constitute a unique component of the immune system that regulates immune responses in healthy individuals and in the context of various diseases. In this Review, we discuss the origin, mechanisms of expansion and suppressive functions of MDSCs, as well as the potential to target these cells for therapeutic benefit.

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Cannabis May Suppress Immune System

Could Lead to New Autoimmune Disorder Treatments, Say Researchers

April 15, 2003 -- Cannabis may offer hope to people with autoimmune disorders such as lupus and rheumatoid arthritis. Cannabis seems to decrease inflammation in the body by suppressing certain parts of the immune system.
Researchers are hoping this finding will lead to new treatments.

Previous studies have hinted at immune system abnormalities among cannabis users -- specifically, in the function of immune system cells called T lymphocytes and natural killer cells. While these cells help the body fight infections, no direct link with lowered immunity has yet been shown.

In this study, researchers tested the blood of 29 cannabis smokers -- 13 occasional users and 16 regular users (weekly or daily use). They compared the results with a group of 32 nonsmokers.

Again, researchers found that cannabis smokers had fewer immune-enhancing natural killer cells and lymphocytes, and higher levels of a protein that may promote tumor growth, called interleukin-10.

These changes can dampen the immune system's response to

infection,
increasing susceptibility to infections and promoting growth of tumors,
states lead researcher Roberta Pacifici, PhD, with the Instituto Superiore
di Sanita in Rome, Italy.

But researchers also say this finding could lead to new treatments for
people with autoimmune disorders. Current treatments suppress the immune
system -- thereby calming the abnormal immune response that plagues people
with the conditions.

Cannabis lowers levels of the inflammation-promoting protein interleukin-2
and raises levels of the anti-inflammatory protein interleukin-10. Both of
these findings could be of potential benefit for treating autoimmune
disorders one day.