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"HIV depletes T-helper17, we simply stimulate it"

By Prof. Dr.Pichaet Wiriyachitra Ph.D., F.R.A.C.I.

HIMSS AsiaPac15
DIGITAL HEALTHCARE WEEK
HIMSS AsiaPac15 Conference & Exhibition
6-10 September 2015, Marina Bay Sands, Singapore
Organised by: HIMSS Asia Pacific

Natural Healthcare for HIV infected – "HIV depletes T-helper17, we simply stimulate it"

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Chairman and CEO, Professor
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LIV: APCO's solution for HIV patients

Background information on HIV

- Once a patient is infected with HIV, the virus penetrates into the white blood cells, known as CD4 cells, which are responsible for boosting the immune system.
- The virus then destroys those CD4 cells and moves to destroy other CD4 cells.
- The HIV virus hides in white blood cells making it difficult to detect and kill.

The type of CD4 cell that HIV destroys most is Th17 which is an essential part of the immune system.

Background information on HIV

HIV patients do not die of HIV. Because their immune system is weakened, they will be susceptible to other opportunistic infections caused by bacteria, fungi and other viruses.

To effectively treat HIV patients,
their CD4 cells need to be restored to a normal level,
and the HIV virus needs to be completely destroyed .

Background information on HIV

- Currently HIV patients are treated with antiretroviral drugs that reduce the HIV virus.

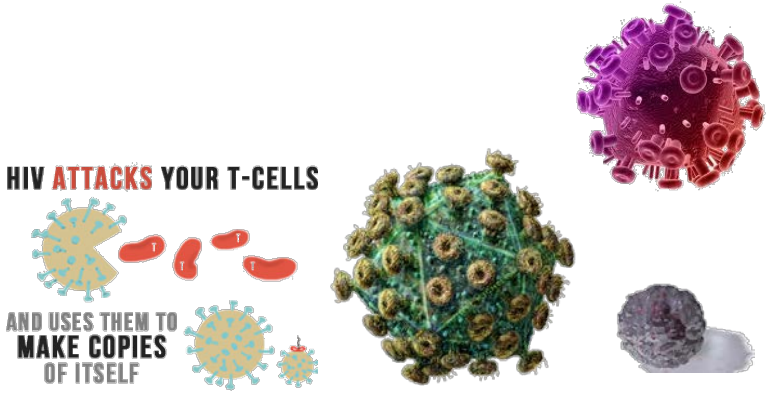
- The antiretroviral drugs have some limitations:
  - They do not help the patients rapidly repair their immune system by restoring their CD4 cells.
  - They cause various side effects in users such as rashes, hives nausea and fevers.

Background information on HIV

Research results from 2012-2013 found that the CD4 cell which is most depleted by the HIV virus are Th17 cells.

1. http://europepmc.org/articles/PMC2999911/

2. http://www.ncbi.nlm.nih.gov/pubmed/21660450



Research shows that increasing Th17 activity can help control the spread of HIV

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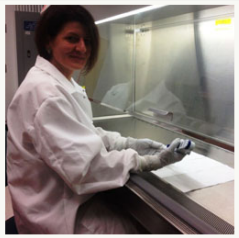
Increasing Th17 Cells in the Gut May Improve the Control of HIV Growth

June 11, 2012 by Staff — Biology

A new study from a team of microbiologists and immunologists suggests that treatment aimed at increasing Th17 cells in the gut may improve the control of HIV growth by promoting an environment in which T cells having more anti-viral capabilities are produced.



Kristina Abel, PhD

Chapel Hill, North Carolina – The findings of a new study in monkeys may help clarify why some people infected with HIV are better able to control the virus. They also may pinpoint a target for treatment during early HIV infection aimed at increasing the supply of certain immune cells in the gut, which the study shows could be an important factor in limiting HIV growth in cells throughout the body.

The study was led by researchers at the University of California, San Francisco (UCSF) and included Kristina Abel, PhD, an assistant professor in the department of microbiology & immunology at UNC, at the time of the study a faculty member at the University of California, Davis (UCD). "The research involved a rhesus macaque model of HIV, monkeys who were infected with simian immunodeficiency virus, SIV" Abel said. "The course of SIV infection in these monkeys is quite similar to that of HIV in humans."

Both HIV and SIV infections cause severe CD4 T cell loss in the gut during early infection. As a result, the intestinal mucosal barrier, which is like the body's second skin or front line of defense against pathogens, is compromised. The "leaky gut" causes bacteria that are normally located in the gut (the normal flora) to migrate out and activate the immune system throughout the body with disastrous health consequences. "The immune activation contributes to higher replication of the virus. And so the question is, why do some patients progress from infection to AIDS faster than others?" Abel asks.

This new study looked at the balance between certain immune cell populations that might influence disease outcome. The study shows the presence of a subtype of CD4-positive immune cells called Th17 (T helper 17) cells in the gut "could influence disease outcome."

A report of the research appeared in the May 30, 2012 on-line issue of Science Translational Medicine. Th17 cells are commonly found at mucosal surfaces and activate epithelial or outer layer barrier cells to secrete antimicrobial molecules, thus blocking disease-causing bacteria from entering. Abel points out that they also stimulate the production of "tight junction" proteins that keep all the cells that make up the intestinal barrier in close contact, "so that bacteria of the normal flora or their products cannot leak out."

The researchers wondered if there are more Th17 cells in the gut, would infection with the AIDS virus still have that early massive effect on gut permeability? And if you could keep the intestinal barrier intact during early infection with HIV, would it have an impact on the severity of disease progression, on having less severe disease in the long run?

Results of the study suggest that the answers may be yes. Rhesus macaques with higher numbers of Th17 cells in blood and intestinal tissue before they are infected with SIV subsequently have lower SIV viral loads. "It appears they're more able to control the infection," Abel said.

The study also found that among animals given a drug that increases regulatory T cells and thereby suppresses Th17 cell development, disease progression occurred more rapidly, and they had higher levels of SIV virus six months after infection.

"The main message of the study is that the frequencies of certain immune cell populations in the normal, still uninfected individual are important in subsequent disease progression and outcome," Abel said. "The paper also suggests that treatment aimed at increasing Th17 cells may improve the control of HIV growth by promoting an environment in which T cells having more anti-viral capabilities are produced."

The study's principal investigator was Dennis J. Hartigan-O'Connor, MD, PhD, from UCSF (now at UCD). Other investigators are Koen K.A. Rompay, from UCD; Bitoo Kanwar, from UCSF; and study senior author Joseph M. McCune, MD, PhD, from UCSF.

Support for the research came from the National Institutes of Health, the Bill and Melinda Gates Foundation, the California National Primate Research Center, the National Center for Research Resources, and the Harvey V. Berneking Living Trust.

Source: UNC Health Care

Image: UNC Health Care

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disease, health, HIV, immune system, immunology, microbiology, UNC Health Care

http://scitechdaily.com/increasing-th17-cells-in-the-gut-may-improve-the-control-of-hiv-growth/

Th17 as a vaccine

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Home > UCSF Researchers Identify A Potential New HIV Vaccine/Therapy Target

UCSF Researchers Identify A Potential New HIV Vaccine/Therapy Target

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By Jeff Sheehy on May 30, 2012

Email

After being infected with simian immunodeficiency virus (SIV) in a laboratory study, rhesus macaques that had more of a certain type of immune cell in their gut than others had much lower levels of the virus in their blood, and for six months after infection were better able to control the virus.

SIV is a retrovirus that infects primates. Strains of SIV that crossed over to humans resulted in the evolution of HIV. In rhesus macaques, SIV causes simian AIDS (though in many primates it is harmless) and studying the virus in these animals offers crucial insights into how HIV acts in humans, the researchers said.

The discovery by researchers at UCSF may shed light on the mystery of why some people infected with HIV are better able to control the virus, live longer and have fewer associated health problems than others who have been infected as long, they said. It also provides a potential new target for developing therapies or vaccines.

The cells that have the protective effect, called Th17 (T helper 17) cells, are a subset of the type of disease-fighting immune cell targeted and killed by HIV and found in the gut of both primates and humans.

A prior study from the same UCSF team found that SIV infection causes a normally protective immune response to infection to go awry, leading to reduction in the protective activity in the gut of these Th17 cells and weakening of mucosal defenses against bacteria. Interestingly, in that study, Th17 cells were not affected by SIV in another primate, African green monkeys, in which SIV infection is harmless and does not cause disease.

Joseph M. McCune, MD, PhD

"Animals with more of these Th17 cells were better able to control SIV and this was due in part to macaques developing a more effective immune response by producing more SIV-specific CD4-positive T-cells to fight the infection. Our next step is to see if we can augment the Th17 effect, perhaps by looking at interleukin 17 (IL-17), the cytokine released by these cells, and testing to see if it has an effect," said the study's primary investigator, Dennis Hartigan-O'Connor, MD, PhD, assistant professor of medicine at the UCSF Division of Experimental Medicine.

"Further, if a treatment can be developed to increase Th17 cells in the gut, it may allow for a more effective immune response after exposure to an HIV vaccine or the virus itself," he added.

The findings are being published in the May 30, 2012 issue of *Science Translational Medicine*.

In the new study, the investigators first determined the levels of Th17 cells in the gut of sixteen rhesus macaques and then infected them with SIV. They found that the animals with more Th17 cells to begin with were better able to control the virus. They then gave animals drugs that deplete Th17 cells and found that reducing the number of Th17 cells made controlling SIV more difficult for those animals.

"We found great variation in the levels of Th17 cells, with as much as a five-fold difference in numbers between animals. e are not sure why this is the case. It could be genetically determined or perhaps due to a previous exposure to a type of bacteria that stimulates production of Th17 cells," said Hartigan-O'Connor.

This study is part of a series of investigations undertaken by researchers at the UCSF Division of Experimental Medicine into how SIV, and by extension HIV, interacts with the immune system in the gut. The previous study was focused on chronic infection and persistent inflammation in the gut.

"The earlier study addressed the cause and consequence of inflammation after infection. We found that inflammation induces an enzyme that knocks out Th17 cells, which normally help to keep the gut intact, and that disease progression was faster. Reciprocally, we have now found that animals do better if they have many Th17 cells at the outset of infection. We are gradually increasing our understanding of this important aspect of the immune system and we are working to translate this understanding into an approach that benefits patients," said study senior author, Joseph M. McCune, MD, PhD, chief of the UCSF Division of Experimental Medicine.

Study co-investigators include Bittoo Kanwar from UCSF Division of Experimental Medicine and Kristina Abel and Koen K. A. Van Rompay from the University of California, Davis.

Funding for this research was provided by the National Institutes of Health, the Bill and Melinda Gates Foundation, the California National Primate Research Center, the National Center for Research Resources and the Harvey V. Berneking Living Trust.

The UCSF Division of Experimental Medicine is affiliated with the AIDS Research Institute (ARI) at UCSF. UCSF ARI houses hundreds of scientists and dozens of programs throughout UCSF and affiliated labs and institutions, making ARI one of the largest AIDS research entities in the world.

UCSF is a leading university dedicated to defining health worldwide through advanced biomedical research, graduate level education in the life sciences and health professions, and excellence in patient care.

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Explore UCSF News

http://www.ucsf.edu/news/2012/05/12083/ucsf-researchers-identify-potential-new-hiv-vaccine-therapy-target

The benefits of LIV capsules

APCO scientists have developed LIV that stimulates Th17, Th1 and Th9 by 5, 2 and 2 folds respectively. All the stimulated Th cells increase the activities of natural killer cells and cytotoxic T-cells that eliminate HIV

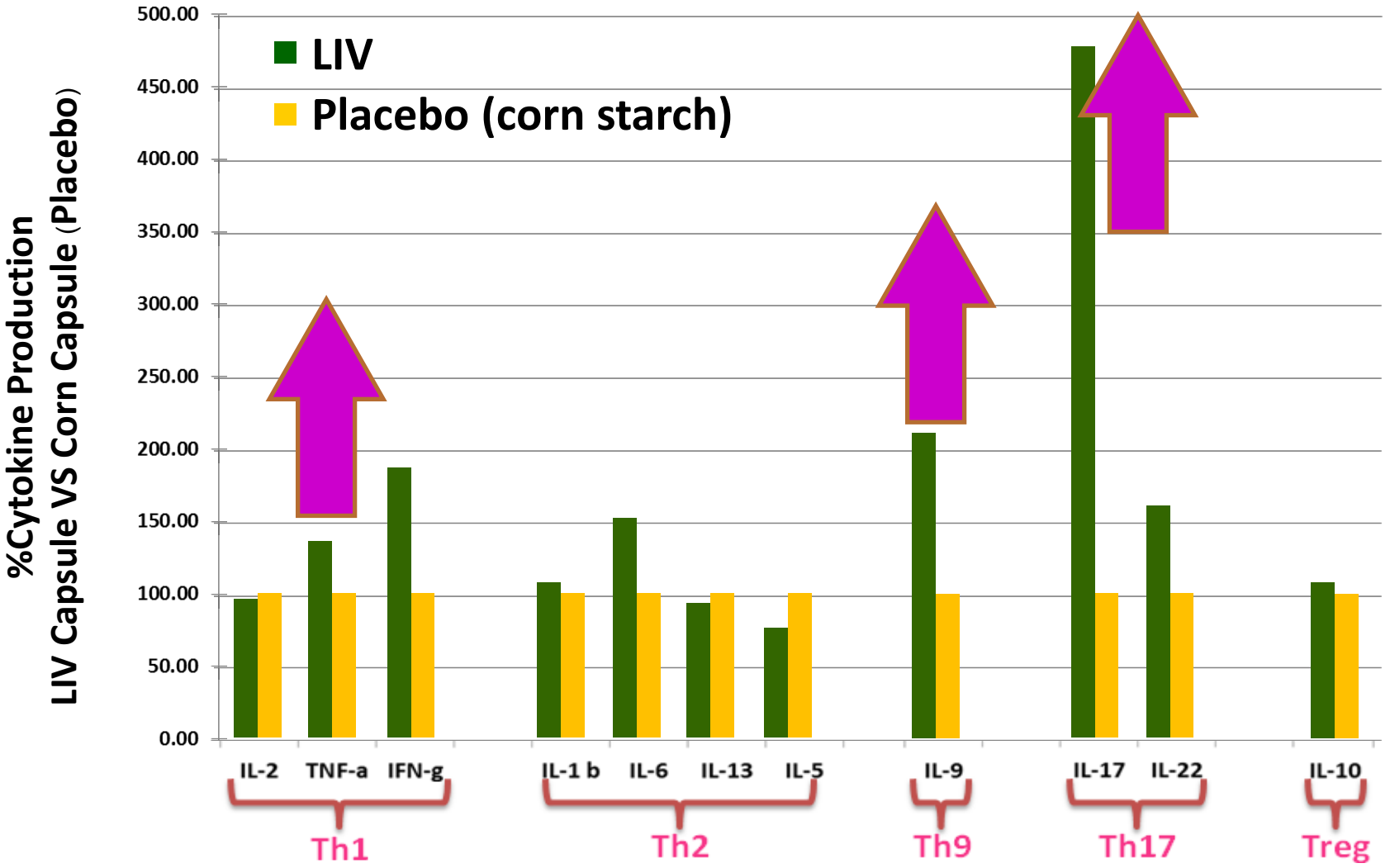
Results of the LIV efficiency test carried out at the Biomedical Technology Research Centre, Chiang Mai University

Healthy volunteers were given 4 LIV capsules a day for 15 days. This resulted in:

- **a five times increase of their Th17 activity.**
- **a doubling of their Th1 and Th9 activity.**

Thus strengthening the immune system to help control the HIV virus.

Scientific Study of the Effects of LIV
4 Capsules a day for 15 days



Increased Th1, Th17 and Th9 enhance the activity of natural killer cells and cytotoxic T cells which will eliminate HIV

Previous research findings

GM-1 in the mangosteen extract used in the LIV capsule inhibits reverse transcriptase and protease enzymes which are essential in the virus replication process.

http://www.ncbi.nlm.nih.gov/pubmed/20492173

Planta Med. 1996. Aug 62(4):381-2

Results of the clinical study of LIV capsules

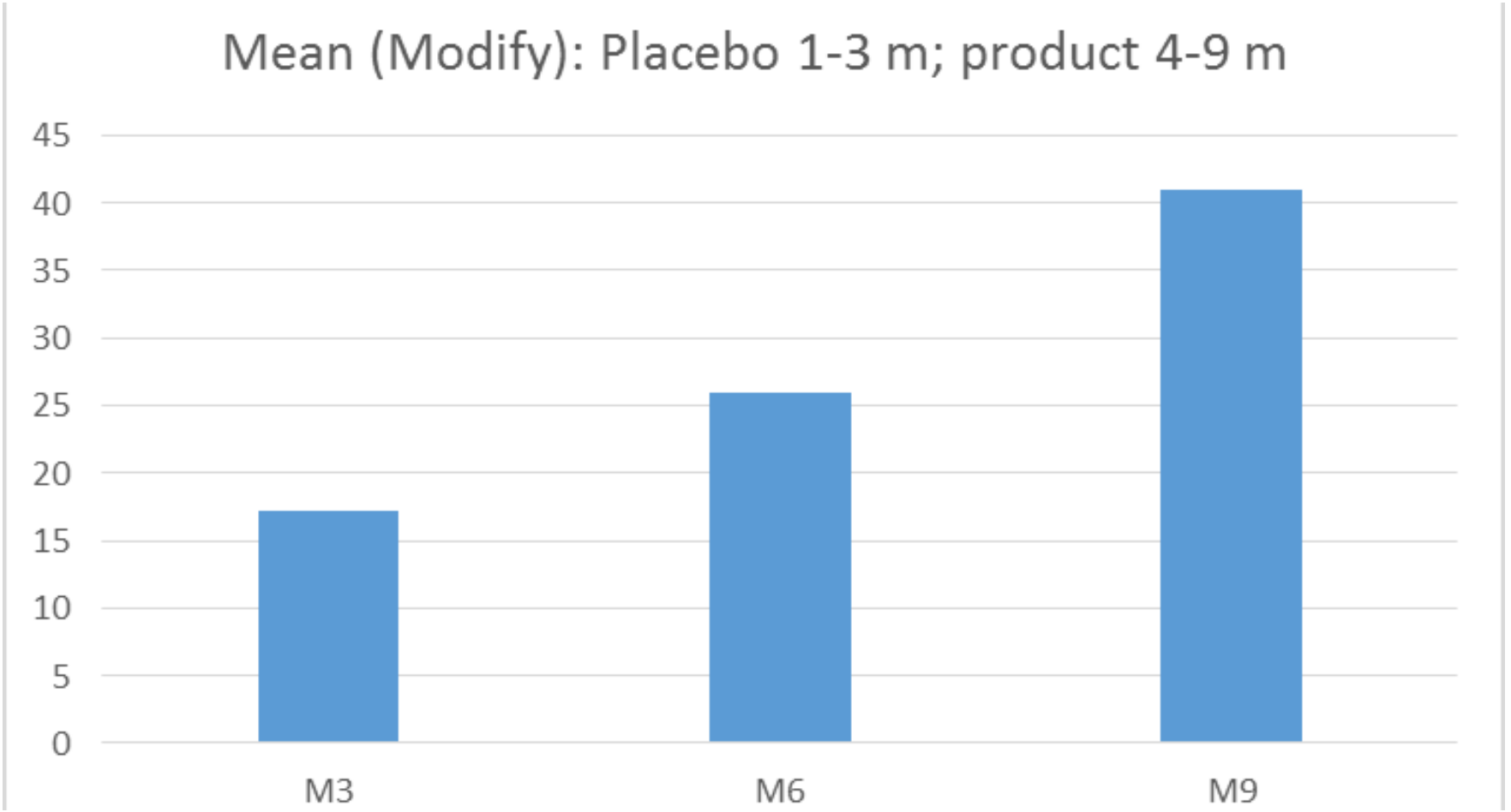
A Chiang Mai University and APCO joint clinical study conducted at Mae-On hospital in Chiang Mai, with the approval of National Science and Technology Development Agency, showed that

1. **The CD4 cell count in HIV patients increased after taking 4 LIV capsules daily for 6-9 months.**

2. **The life quality of all volunteers improved significantly**

APCO has since donated a life-time supply of LIV capsules to the 27 volunteers who took part in this clinical study.

Graphic illustration of % increase of absolute CD4 lymphocyte (cell cu.mm.) in 3, 6 and 9 months.



Results of the Test of LIV Capsules on HIV Infected Patients

APCO has given LIV capsules to HIV-infected volunteers in Chiang Mai who have been taking antiretroviral drugs for two years with the following results:

- Their life quality improved significantly.
- Those suffering from opportunistic infection such as viral infection, tuberculosis and pneumonia saw their symptoms remedied.

APCO has since donated a life-time supply of LIV capsules to the 21 volunteers who took part in this research study.

Increase of CD4 count on volunteers at Doi Saked district

month / sex	CD4 (5/2013-10/2013)								
	0	1	2	3	4	5	6	last	%increase
F(1)	19	50	57	53	40	55	76	89	368.42%
M(1)	108	84	78	111	90	96		137	26.85%
M(2)	192	392	272	257	201	259	217	410	113.54%
F(2)	83		224	106	121	162	142		71.08%
F(3)	413	425	322	446		426			3.15%
M(3)	84		102	115	130	129		169	101.19%
F(4)	179	286	263	187	203				13.41%
M(4)	186	206	149	200	193	190	185	210	12.90%
M(5)	225	166	163	214	201	248	243	543	141.33%
F(5)	245	199	239	174	266	185			-24.49%
M(6)	258	338	298	312	352	318		477	84.88%
M(7)	484	640	387	434	458	539			11.36%
M(8)	422	510	475	359	433	359			-14.93%
M(6)	431	383		353	384			409	-5.10%
F(6)	69	137		101	108				56.52%
									64.01%

Improvement of life quality is reported from all volunteers (100%) with 4 capsules/day.

Volunteers with pneumonia F(1) and TB M(2) recovered in less than 1 month with 6 capsules/day

Increase of CD4 count on volunteers at Sarapee district

	CD4 (3/2013 – 1/2015)							7/2014	9/2014	
sex	M1	M2	M3	M4	M5	M6	M11	M17	M19	% Increase
M(1)	392	420	363		467	355	458		538	37.24%
F(1)	385	410	455	486	473	487	382	541	586	52.21%
M(2)	674	714	651	593	642	583	590			-12.46%
F(2)	363	420	312	412	333	355	360		437	20.39%
M(3)	109	134	117	115	131	129		147	135	23.85%
M(4)	467	434	464	500	428	576	518			10.92%
										22.02%

Improvement of life quality is reported from all volunteers(100%)

Test results on children at Baan Gerda

At Baan Gerda Children's Rights Foundation, APCO has given LIV capsules to HIV-infected children who were taking antiretroviral drugs and suffering from opportunistic diseases.

- **After taking 4 LIV capsules a day for 12 months, the opportunistic infection symptoms were remedied and their CD4 count increased by an average of 67.34%.**

- **A group of children who were already taking antiretroviral drugs but whose CD4 count had not increased for the previous 6 months had their CD4 count increased by an average of 32.45% after taking 9 LIV capsules a day for 3 months.**

Increase of CD4 and %CD4 of the additional 50 cases in 6 months

	sex	Age (years)	CD4 (December 2014 – May 2015)						
			M0		M6		Increase (Decrease)		
			Absolute CD4	%CD4	Absolute CD4	%CD 4	Absolute CD4		%CD4
								%	
1	M	6	642	26	935	32	293	45.64%	6.00
2	F	8	897	25	1,334	32	437	48.72%	7.00
3	F	10	340	18	759	28	419	123.24%	10.00
4	F	12	1,075	35	1,814	42	739	68.74%	7.00
5	M	12	920	25	820	26	-100	-10.87%	1.00
6	M	13	822	25	863	30	41	4.99%	5.00
7	F	14	680	34	963	37	283	41.62%	3.00
8	M	14	564	31	917	37	353	62.59%	6.00
9	M	14	560	22	1,123	30	563	100.54%	8.00
10	M	14	400	23	969	27	569	142.25%	4.00

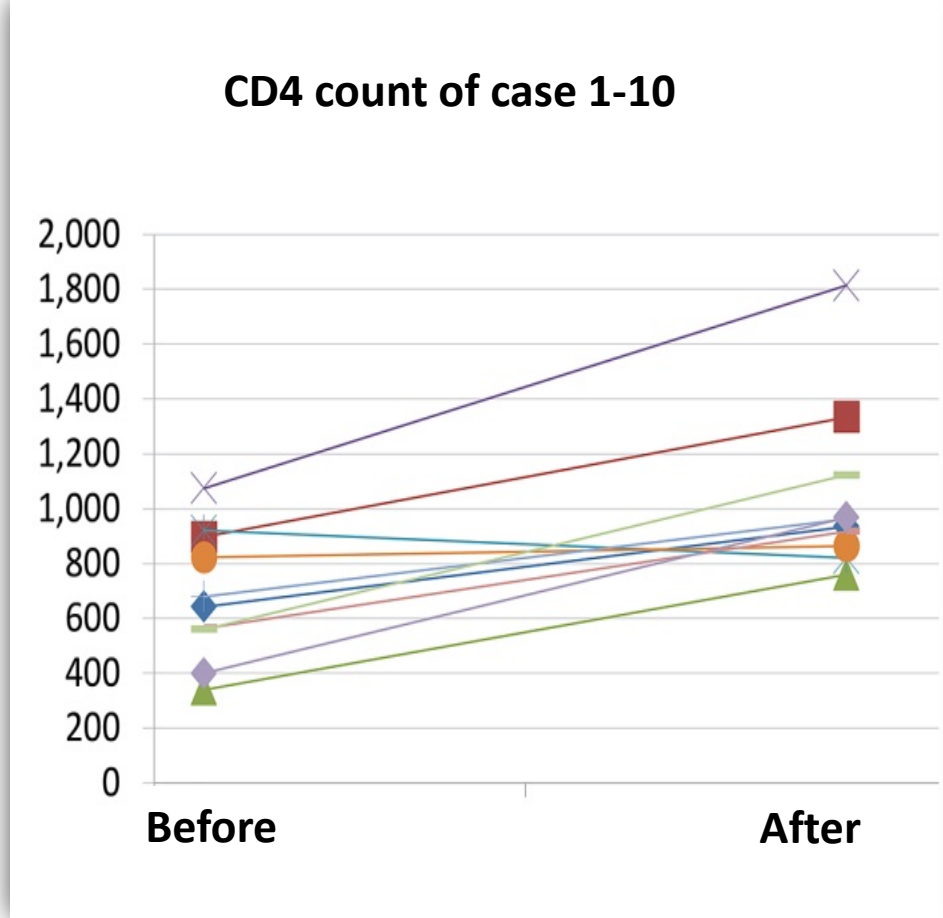
	sex	Age (years)	CD4 (December 2014 – May 2015)						
			M0		M6		Increase (Decrease)		
			Absolute CD4	%CD4	Absolute CD4	%CD 4	Absolute CD4		%CD4
								%	
11	M	14	559	32	530	35	-29	-5.19%	3.00
12	M	14	670	21	777	23	107	15.97%	2.00
13	M	14	1,537	36	1,669	36	132	8.59%	0.00
14	M	14	915	30	762	33	-153	-16.72%	3.00
15	M	15	414	25	722	28	308	74.40%	3.00
16	M	15	397	32	837	35	440	110.83%	3.00
17	F	15	291	21	544	26	253	86.94%	5.00
18	M	15	678	20	877	32	199	29.35%	12.00
19	M	15	465	21	1,037	26	572	123.01%	5.00
20	F	15	374	25	605	24	231	61.76%	-1.00

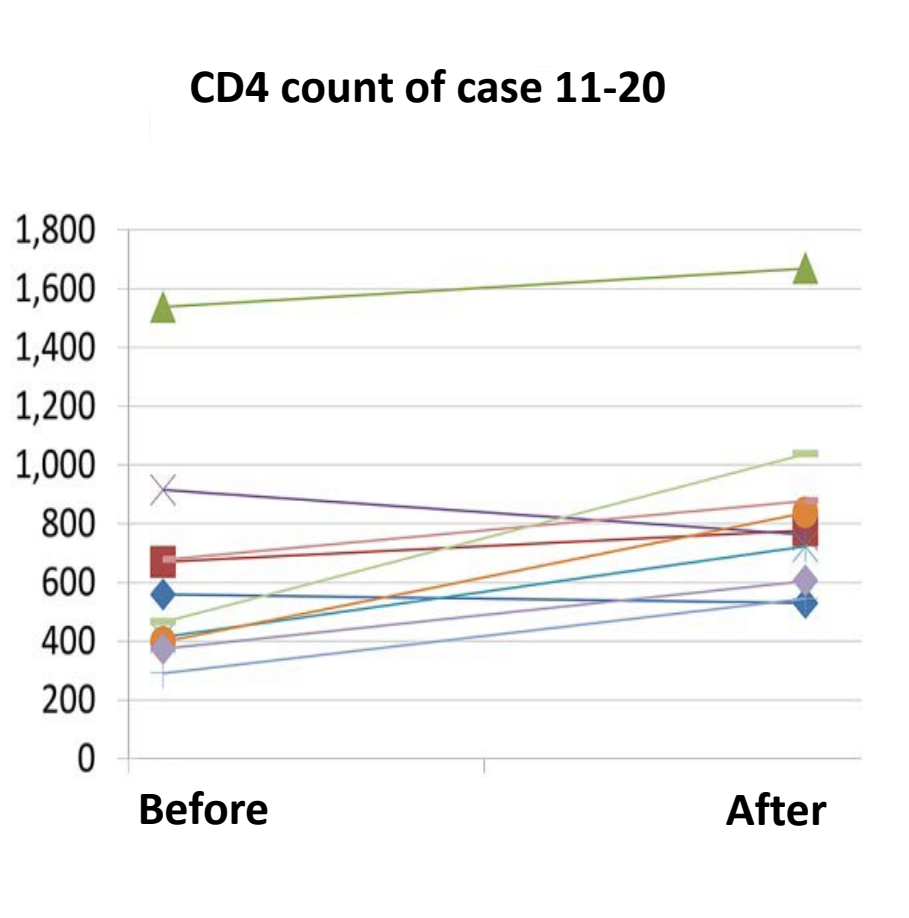
	sex	Age (years)	CD4 (December 2014 – May 2015)						
			M0		M6		Increase (Decrease)		
			Absolute CD4	%CD4	Absolute CD4	%CD4	Absolute CD4		%CD4
								%	
21	F	15	870	33	951	32	81	9.31%	-1.00
22	M	15	650	19	704	26	54	8.31%	7.00
23	F	15	883	31	909	29	26	2.94%	-2.00
24	M	15	957	24	1,002	23	45	4.70%	-1.00
25	F	15	94	4	364	17	270	287.23%	13.00
26	F	16	318	33	1,037	36	719	226.10%	3.00
27	F	16	433	24	629	28	196	45.27%	4.00
28	F	17	416	12	579	16	163	39.18%	4.00
29	M	17	962	32	1516	35	554	57.59%	3.00
30	F	17	535	25	833	34	298	55.70%	9.00

	sex	Age (years)	CD4 (December 2014 – May 2015)						
			M0		M6		Increase (Decrease)		
			Absolute CD4	%CD4	Absolute CD4	%CD4	Absolute CD4		%CD4
								%	
31	F	17	640	24	1,084	37	444	69.38%	13.00
32	M	17	666	35	1,193	45	527	79.13%	10.00
33	F	17	499	22	733	25	234	46.89%	3.00
34	F	17	841	33	1,347	37	506	60.17%	4.00
35	F	17	450	26	919	32	469	104.22%	6.00
36	F	17	325	18	520	24	195	60.00%	6.00
37	F	17	1, 161	35	1,438	40	277	23.86%	5.00
38	F	17	554	18	750	20	196	35.38%	2.00
39	M	18	560	26	942	25	382	68.21%	-1.00
40	F	18	407	15	660	17	253	62.15%	2.00

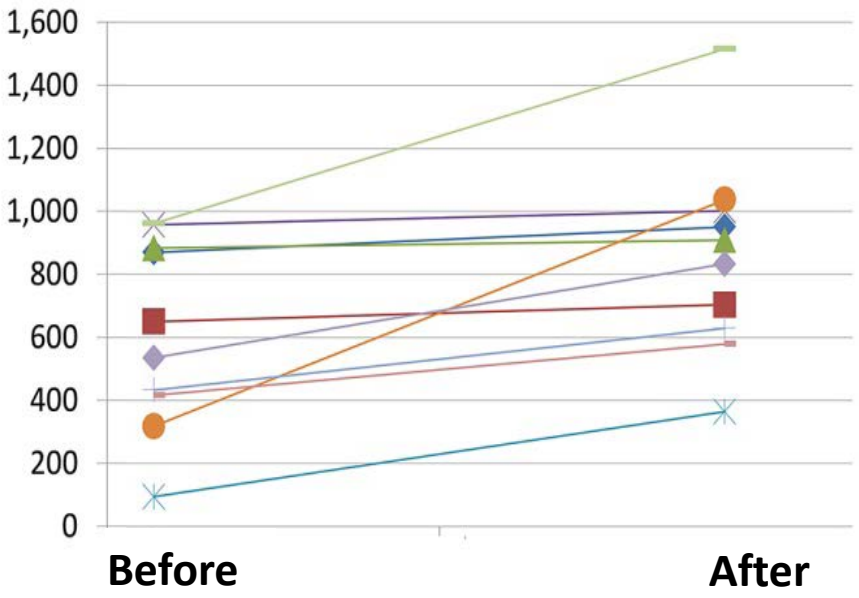
	sex	Age (years)	CD4 (December 2014 – May 2015)						
			M0		M6		Increase (Decrease)		
			Absolute CD4	%CD4	Absolute CD4	%CD4	Absolute CD4		%CD4
								%	
41	F	18	519	30	1,169	40	650	125.24%	10.00
42	M	18	977	24	1,141	24	164	16.79%	0.00
43	F	18	841	23	1,028	28	187	22.24%	5.00
44	M	19	825	26	1,235	31	410	49.70%	5.00
45	M	20	668	27	895	33	227	33.98%	6.00
46	F	33	866	27	1,374	33	508	58.66%	6.00
47	F	36	859	26	1,090	32	231	26.89%	4.00
48	F	39	387	22	864	26	477	123.26%	3.00
49	F	41	641	26	844	29	203	31.67%	3.00
50	M	41	396	20	574	26	178	44.95%	6.00
					Average			59.91%	4.64

Increase of CD4 count of the additional 50 cases in 6 months

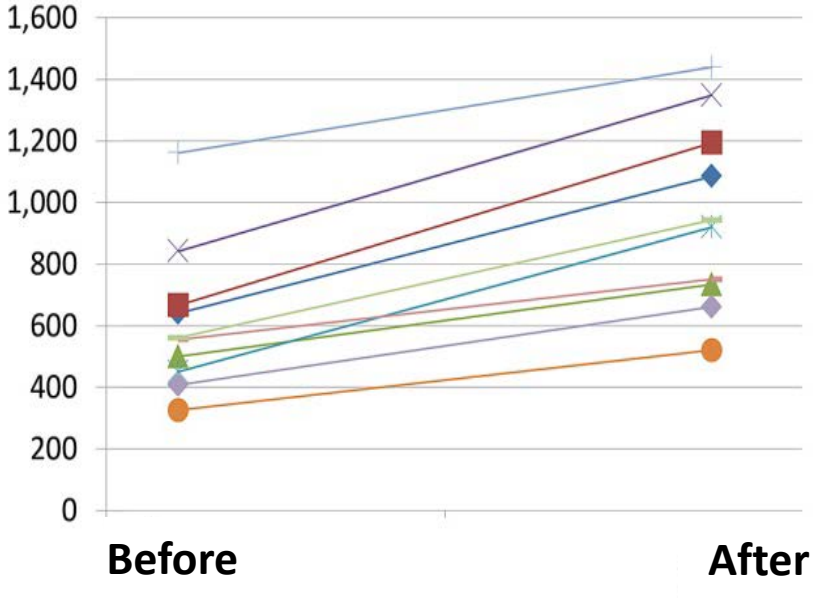


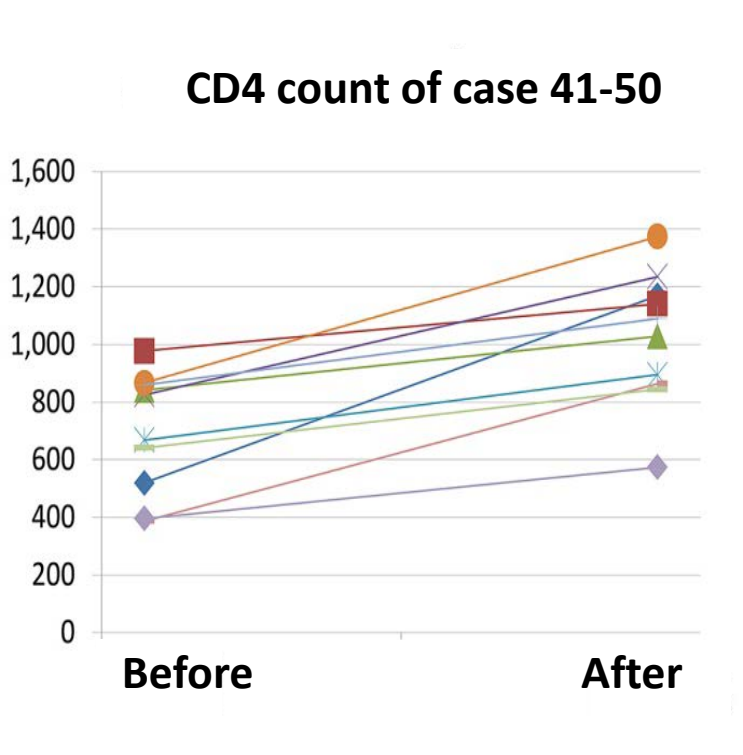


CD4 count of case 21-30



CD4 count of case 31-40





Average CD4 increases 59.91%
%CD4 increases 4.64%
Improvement seen in all cases (when combined CD4 count and %CD4 are considered)

APCO has since planned to provide a life-time supply of LIV capsules to all the 70 children infected with HIV at Baan Gerda.

Now, all 70 children at Baan Gerda

1. have the improve life-quality
2. have the normal CD4 count
3. have the below detectable level of viral load (20 copies/ml)

Case study of a volunteer who has not used antiviral drug

	CD4 (%)	CD4 cells/cu.mm	Viral Load copies/ml
Before using LIV frequent headache, loss of sleep, rash and irritation on skin.	18.70	418.60	8,814
month 1-3, 4 capsules/day healthier, rash and irritation gone.	27.00	546.00	34,462
month 4-6, 9 capsules/day healthier, better appetite, sleep well, no more headach.	22.00	560.00	31,919
month 7-9, 9 capsules/day very healthy, better appetite, sleep well.	20.00	474.00	6,985
month 10-12, 9 capsules/day very healthy, good appetite, sleep well.	25.00	668.00	<40
Normal average of healthy people	26-40	538-922	0

LIV Best Result

1. In the group of patients who were taking antiviral drugs

1 patient took LIV in 1 month

- CD4 count increased from 94 to 364 cells/mm^3,
- %CD4 increased from 4% to 17%,
- Viral load decreased from 1,090,000 to 850 copies/ml.

LIV Best Result

2. In the group of patients who were taking antiviral drug and had opportunistic infections.

1 patient could not cure TB infection by drugs, but gained more strength and resumed normal life within 2 weeks by LIV.

LIV Best Result

3. Patient who was not taking antiviral drug but only LIV.

His CD4 count increased to normal range and viral load decreased below 40 copies/ml in 12 months.

Benefits of LIV Capsule

1. LIV capsule rapidly increases patients' CD4 count.
2. LIV capsule stimulates Th1,Th9 and Th17 that can lead to the elimination of HIV virus.
3. LIV capsule remedies the opportunistic infection symptoms by boosting the patients' immune systems.
4. LIV capsule reduces the side effects caused by antiretroviral drugs.
5. LIV capsule improves the quality of life of HIV patients, enabling them to live normal lives.

4 September 2015

National Innovation Agency

recognized LIV capsule as

the innovative products of Thailand

for improving the life quality of HIV infected

สำนักงานนวัตกรรมแห่งชาติ

NATIONAL INNOVATION AGENCY

สำนักงานนวัตกรรมแห่งชาติ
National Innovation Agency

Statement of Recognition

The **National Innovation Agency (Public Organization)** ("NIA") is a Thai government entity that promotes and supports innovation development in Thailand. NIA issues this statement in due regard to innovative products by **Asian Phytoceuticals Public Company ("APCO")**, led by its CEO, Prof. Dr. Pichaet Wiriyachitra, as follows:

1. NIA acknowledges the achievement of APCO in successfully researching and developing "APCO cap"*, an innovative product which is aimed to improve the quality of life of HIV infected people globally.

2. NIA has learned that APCO recently completed the development of "APCO cap" and has marketed it globally under various brands. The product has been registered with the Thai FDA as a dietary supplement. APCO asserts that the product is manufactured from a synergistic mixture of extracts from mangosteen, sesame, soy, guava and Centella.

3. NIA has been informed that APCO, a company listed on the **mai** Stock Exchange of Thailand, was also the recipient of the **mai** Best Company Performance Award 2014, Most Improved CSR Award 2014 and was voted by Forbes Magazine as one of the Asian 200 Best Under a Billion with the market cap of $2.1 billion as of June 2015. NIA acknowledges that APCO is a technologically advanced company that specializes in the research, development, manufacture and promotion of health and cosmetic products made from natural plant extracts.

4. NIA also recognizes the achievements of the multidisciplinary research team led by Prof. Dr. Pichaet Wiriyachitra, the company's CEO who recently received the **mai** Best CEO Award 2014, CST Award for Distinguished Contribution to Economic Advancement 2014 from Thai Chemical Society and Australian Alumni of the Year Award 2015.

*www.livcapsules.com (English), *www.livcapsule.com (Thai)

According to the foregoing, NIA recognizes "APCO cap" as a Thai innovative product.

Associate Professor Dr. Somchet Thinapong
Chairman of the National Innovation Board

4/9/'15
Date

Dr. Pun-Arj Chairatana
Director

4/09/'15
Date

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