



No Fear on Cancer and The Other Diseases --- Another Choice with Huaier.

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Abstract

Among historical nature remedies in Eastern Asia, Huaier has long been reported for its significant efficacy on longevity and health maintenance, and more importantly, on cancer. The present study initiated to identify the main controlling mechanism integrating a broad effect of Huaier, with a consideration into its characteristics according to the cell-type and tissue specificity. In addition, spontaneous SARS-CoV-2 production has been identified after Pfizer-BioNTech mRNA vaccination, observed from 3 weeks after first injection until even at 5 months after 3rd vaccination with progressively destructive ribosomal RNAs. Huaier administration also recovered the destructive effects also observed in the patients with conventional chemotherapy. Molecular basis demonstrated were dependent on genomic potential to rescue the functional control on perturbed kinase regulation through the integrated mTOR/PI3K/AKT pathway network, with the massive mi- and piRNA-mediated transcriptional control. Huaier might play a key role to reset the genome potential in each individual through embryonic stem cells or various progenitor cells, and restart the regeneration process toward normal cell proliferation and specification process. Thus the efficacy of Huaier can provide a solution to a broad range of transcriptional dysregulation diseases not only via Hippo pathway control, but also multiple integrated signal transfer systems. especially functioning as tyrosine kinase regulator. The time has come to mankind, finally we reached the time when we do not need to fear the threat of cancer at last.

Keywords: Huaier (*Trametes robiniophila murr*); complementally cancer therapy; ribosomal RNA structure; KEGG signaling pathway characterization; miRNA-mediated transcription control; intra/inter neural communication; tyrosine kinase signaling pathway.

In this review, I would like to introduce Chinese natural herb, Huaier, for successful cancer recovery and health maintenance. Please send me your opinions and questions later by e-mail or Telephone call. Later, I will reply with detailed information.

In addition, I would like to emphasize the observed influences of the repeated mRNA vaccinations against SARS-Cov-2.

ADDITIONAL:

Huaier effects on functional compensation with destructive ribosomal RNA structure after anti-SARS-CoV-2 mRNA vaccination.

Huaier effects on prevention and inhibition of spontaneous SARS-CoV-2 virion production by repeated Pfizer-BioNTech mRNA vaccination.



What is natural Herb: Huaier?

Jpn. Trade Name: Kaiji

Chinese Trade Name: Huaier

(Chinese administration license No. Z-20000109)

Species: *Trametes robiniophila murr*

Price: 133 € (3g/ day x 30days) to 1400 € (60g x 30days)

Anti-cancer drug (trade name): KRESTIN

Species: *Trametes versicolor* strain CM-101

MW 9.4×10^4

Content: Coriolan contains polysaccharides (β -glucans); Glucose (74.6%),

Mannose (15.5%), Xylose (4.8%), Galactose (2.7%), Fucose (2.4%), and etc.



Price: 272 € (3g/ month) , 40years of KRESTIN efficacy
= 1.5 years' Huaier

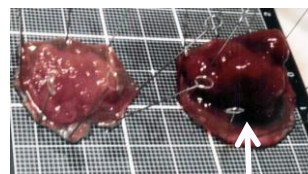
First, what is Huaier? There is a long history on Huaier, first appeared in the literature described at B.C. 200. A result from a long trip to find the natural herb in Xin dynasty. Currently, Huaier can be cultivated, and enough quantity prepared for clinics. It costs very expensive, although efficacy depends on quantity, and not yet covered by National Insurance in Japan.

Huaier Effects on Colon Cancer Two lesions dissected by colon-endoscope

**Lesions at diagnosis
3 months before dissection**



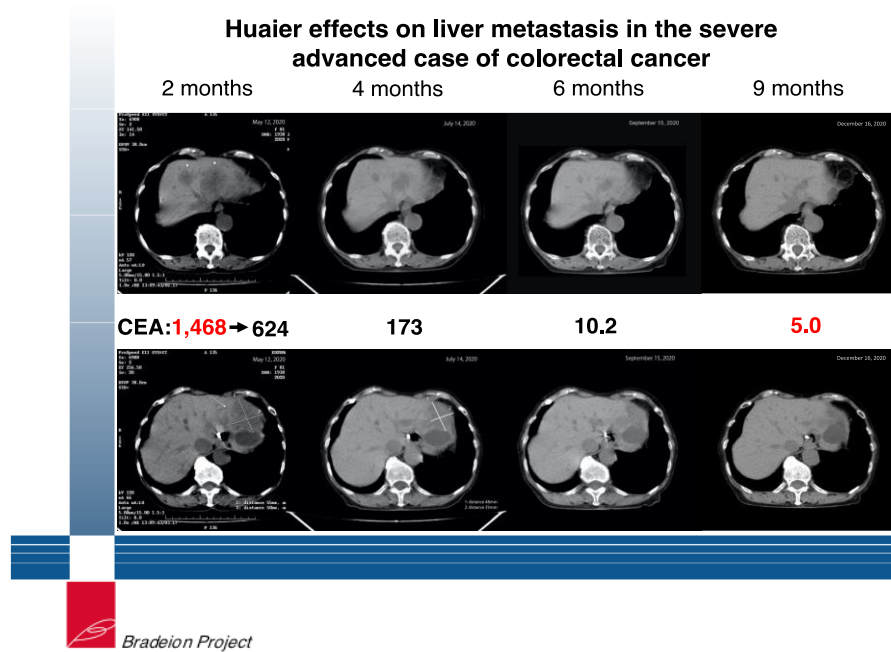
**2 weeks Huaier treatment
Decreased width x depth**



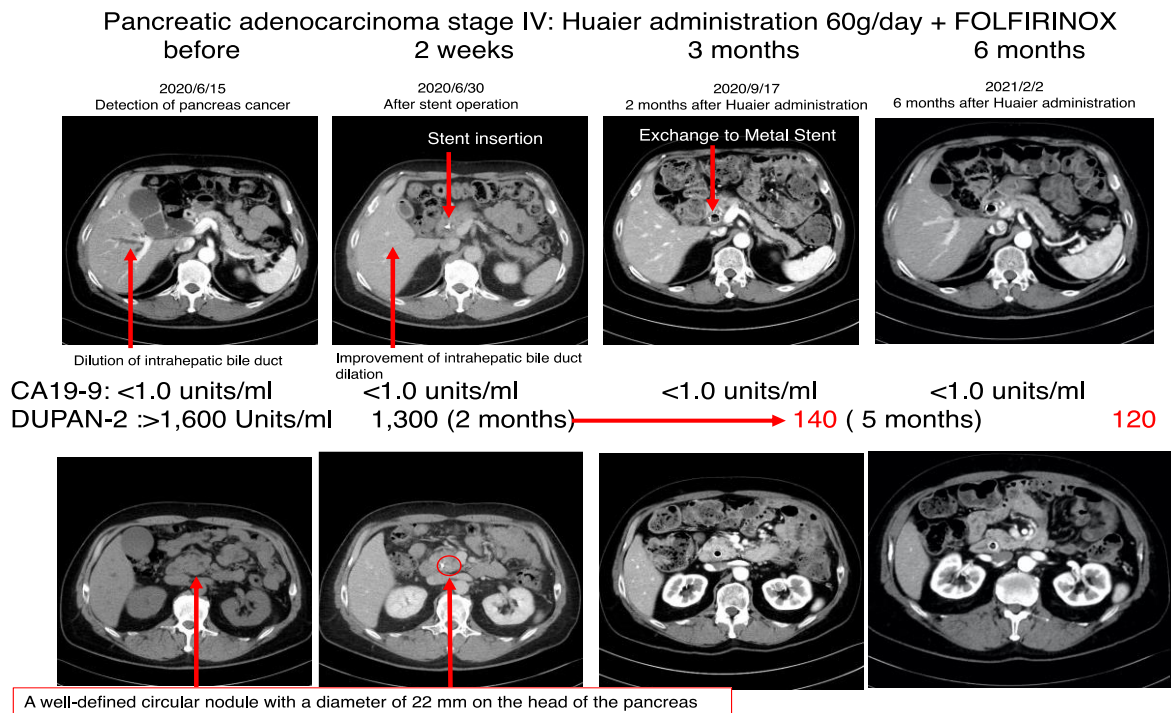
Massive necrosis



Let me show the typical anti-cancer effects of Huaier. The successful dissection by endoscope was performed after 2 weeks of Huaier treatment. See massive necrosis of the cancer lesion at the time of dissection.



Huaier effects on liver metastasis in the severe advanced case of colorectal cancer. The recovery can be seen by CT image, together with significant decrease of tumor marker CEA. Within one year, the patient was recovered completely.

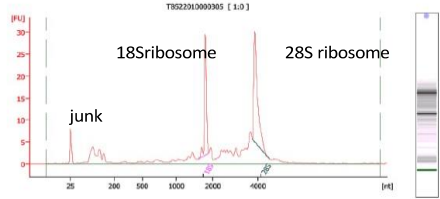


Huaier effects on pancreatic cancer, surgical detection not applicable, multiple metastasis in the liver and both lungs. 60 grams per day Huaier treatment resulted in significant decrease of cancer cells, also judged by tumor marker titers. The patient successfully dissected pancreatic lesion and metastatic lesion, and currently no problem after four years

Destructive Effects of Conventional chemotherapy with platinum (II) complex to Ribosomal RNA Structures

Oesophageal squamous cell carcinoma: Stage IV

Pancreatic adenocarcinoma stage IV

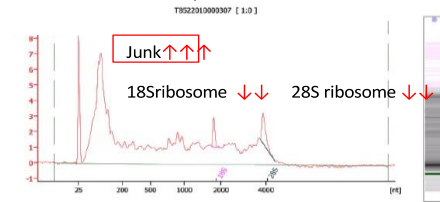


Overall Results for sample 1 : T8522016000305
 RNA Area: 165.5 RNA Integrity Number (RIN): 8.4 (0.0297)
 RNA Concentration: 123 ng/ul Result Flagging Color: OK
 rRNA Ratio (28s / 18s): 1.4 Result Flagging Label: RIN 8.46

Fragment table for sample 1 : T8522016000305

Name	Start Size [nt]	End Size [nt]	Area	% of total Area
18S	1,502	1,890	22.3	13.4
28S	3,741	4,959	33.1	19.3

↓
 cisplatin : CDDP
 one year

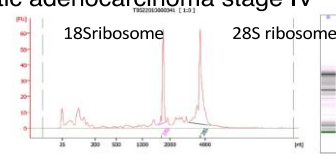


Overall Results for sample 2 : T8522016000307
 RNA Area: 131.9 RNA Integrity Number (RIN): 3.1 (0.0207)
 RNA Concentration: 68 ng/ul Result Flagging Color: NG
 rRNA Ratio (28s / 18s): 1.7 Result Flagging Label: RIN 3.10

Fragment table for sample 2 : T8522016000307

Name	Start Size [nt]	End Size [nt]	Area	% of total Area
18S	1,291	2,022	5.4	4.2
28S	3,726	4,430	2.7	2.0

Before

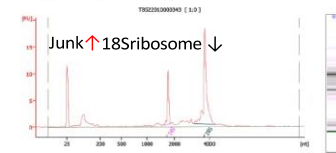


Overall Results for sample 7 : T8522016000341
 RNA Area: 85.9 RNA Integrity Number (RIN): 8.9 (0.0247)
 RNA Concentration: 162 ng/ul Result Flagging Color: OK
 rRNA Ratio (28s / 18s): 2.9 Result Flagging Label: RIN 8.91

Fragment table for sample 7 : T8522016000341

Name	Start Size [nt]	End Size [nt]	Area	% of total Area
18S	1,502	1,891	46.1	53.7
28S	3,098	4,396	39.4	46.3

FOLFIRINOX
 Huaier 60g
 30 days

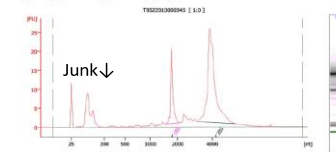


Overall Results for sample 8 : T8522016000342
 RNA Area: 65.4 RNA Integrity Number (RIN): 6.5 (0.0247)
 RNA Concentration: 68 ng/ul Result Flagging Color: OK
 rRNA Ratio (28s / 18s): 3.1 Result Flagging Label: RIN 6.51

Fragment table for sample 8 : T8522016000342

Name	Start Size [nt]	End Size [nt]	Area	% of total Area
18S	1,279	1,623	2.1	3.2
28S	3,091	4,307	25.1	38.7

FOLFIRINOX
 Huaier 60g
 90 days



Overall Results for sample 9 : T8522016000343
 RNA Area: 186.4 RNA Integrity Number (RIN): 9.0 (0.0227)
 RNA Concentration: 194 ng/ul Result Flagging Color: OK
 rRNA Ratio (28s / 18s): 3.3 Result Flagging Label: RIN 9.01

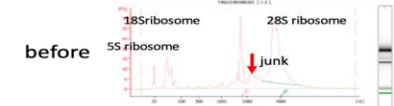
Fragment table for sample 9 : T8522016000343

Name	Start Size [nt]	End Size [nt]	Area	% of total Area
18S	1,339	2,122	20.1	10.8
28S	3,137	4,323	165.8	89.2

Here, I make special attention to the destructive effects of conventional chemotherapy compared with Huaier effects. Left panel indicates cisplatin for a year completely destroyed ribosomal RNA structures. In Right panel, Huaier compensates destruction after one month of both conventional chemotherapy and Huaier treatment. The destruction of ribosomal structure means no satisfactory RNA synthesis in new borne cells, which resulted in no tissue regeneration after cancer cell death.

Structure destructions of Ribosome RNA ion new borne cells After anti-COVID mRNA vaccinations (decrease of regeneration)

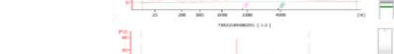
normal control (67 years' old)
 18S/28S ribosome RNA(HPLC)



Overall Results for sample 1 : T8522016000301
 RNA Area: 467.0 RNA Integrity Number (RIN): 8.4 (0.0247)
 RNA Concentration: 171 ng/ul Result Flagging Color: OK
 rRNA Ratio (28s / 18s): 2.2 Result Flagging Label: RIN 8.41

Fragment table for sample 1 : T8522016000301

Name	Start Size [nt]	End Size [nt]	Area	% of total Area
18S	1,502	1,891	100.0	21.4
28S	3,098	4,396	366.0	78.6



Overall Results for sample 2 : T8522016000302
 RNA Area: 467.0 RNA Integrity Number (RIN): 8.4 (0.0247)
 RNA Concentration: 171 ng/ul Result Flagging Color: OK
 rRNA Ratio (28s / 18s): 2.2 Result Flagging Label: RIN 8.41

Fragment table for sample 2 : T8522016000302

Name	Start Size [nt]	End Size [nt]	Area	% of total Area
18S	1,502	1,891	100.0	21.4
28S	3,098	4,396	366.0	78.6



Overall Results for sample 3 : T8522016000303
 RNA Area: 467.0 RNA Integrity Number (RIN): 8.4 (0.0247)
 RNA Concentration: 171 ng/ul Result Flagging Color: OK
 rRNA Ratio (28s / 18s): 2.2 Result Flagging Label: RIN 8.41

Fragment table for sample 3 : T8522016000303

Name	Start Size [nt]	End Size [nt]	Area	% of total Area
18S	1,502	1,891	100.0	21.4
28S	3,098	4,396	366.0	78.6

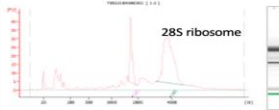


Overall Results for sample 4 : T8522016000304
 RNA Area: 467.0 RNA Integrity Number (RIN): 8.4 (0.0247)
 RNA Concentration: 171 ng/ul Result Flagging Color: OK
 rRNA Ratio (28s / 18s): 2.2 Result Flagging Label: RIN 8.41

Fragment table for sample 4 : T8522016000304

Name	Start Size [nt]	End Size [nt]	Area	% of total Area
18S	1,502	1,891	100.0	21.4
28S	3,098	4,396	366.0	78.6

oesophageal cancer
 3 weeks after 3rd vaccination



Overall Results for sample 5 : T8522016000305
 RNA Area: 467.0 RNA Integrity Number (RIN): 8.4 (0.0247)
 RNA Concentration: 171 ng/ul Result Flagging Color: OK
 rRNA Ratio (28s / 18s): 2.2 Result Flagging Label: RIN 8.41

Fragment table for sample 5 : T8522016000305

Name	Start Size [nt]	End Size [nt]	Area	% of total Area
18S	1,502	1,891	100.0	21.4
28S	3,098	4,396	366.0	78.6

colorectal cancer
 3 weeks after 3rd vaccination
 + Huaier 60g/day for one month



Overall Results for sample 6 : T8522016000306
 RNA Area: 467.0 RNA Integrity Number (RIN): 8.4 (0.0247)
 RNA Concentration: 171 ng/ul Result Flagging Color: OK
 rRNA Ratio (28s / 18s): 2.2 Result Flagging Label: RIN 8.41

Fragment table for sample 6 : T8522016000306

Name	Start Size [nt]	End Size [nt]	Area	% of total Area
18S	1,502	1,891	100.0	21.4
28S	3,098	4,396	366.0	78.6

without Huaier ↓ Conventional
 Chemotherapy




Overall Results for sample 7 : T8522016000307
 RNA Area: 467.0 RNA Integrity Number (RIN): 8.4 (0.0247)
 RNA Concentration: 171 ng/ul Result Flagging Color: OK
 rRNA Ratio (28s / 18s): 2.2 Result Flagging Label: RIN 8.41

Fragment table for sample 7 : T8522016000307

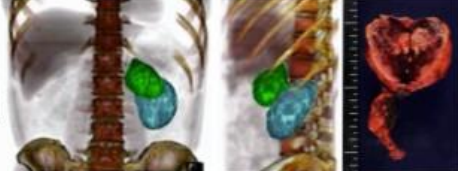
Name	Start Size [nt]	End Size [nt]	Area	% of total Area
18S	1,502	1,891	100.0	21.4
28S	3,098	4,396	366.0	78.6

Examples of ribosomal RNA structures compared with normal control, mRNA vaccination, with or without conventional chemotherapy. This damage of vaccinated normal control was fully recovered by administrating 20 grams of Huaier 3 months. Surprisingly, a gross quantity of hair growth was observed simultaneously. We will further discuss about this normal control data later as Panel A in the last section of this review, relating to the genomic influence of repeated anti-COVID mRNA vaccination.


Breast Cancer Stage 3 (at diagnosis)
Huaier treatment 20g/day) for 1 year
 started at 4 weeks before surgical dissection,
 and cryostat revealed no cancer cells in the dissected
 lesion and lymph nodes



Pituitary Tumor 7 x 9 cm
Huaier treatment 20g/day) for 2 years
 started at 3 months before endoscopic dissection,
 and massive necrosis and cyst formation in the
 dissected tumor



Pulmonary and bone metastasis of colon cancer;
notable bone regeneration




5 months

CEA 10.0 4.6

Tumor mass decreased to 1/8

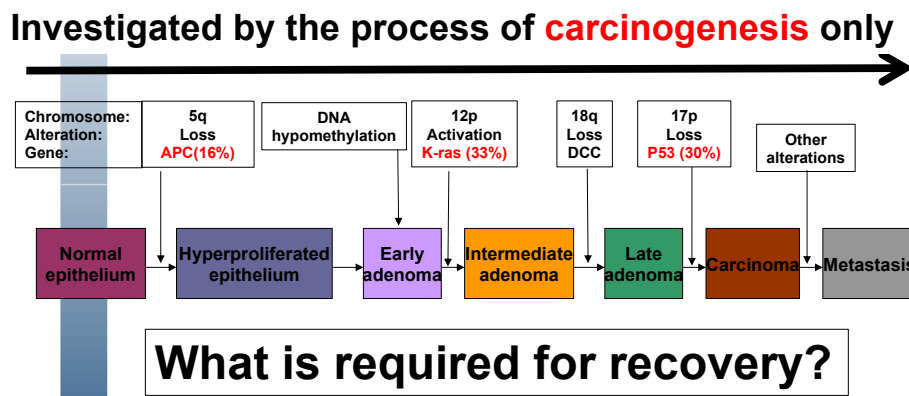
Idiopathic dermatitis after 3 month's steroid
 treatment: Huaier 3g per day for 4 weeks



Melanin pigmentation by steroids

Additional Huaier effects are shown. Huaier effects are dose-dependent. And 3 gram per day is enough to cure dermatitis.

An example of molecular basis for tumorigenesis
 Genetic changes of a typical colon carcinoma
 (Varmus & Weinberg, 1993)



Cancer research has been investigated what happens in the process of carcinogenesis. However, there are scarce information to explain what kind of molecular basis required for cancer recovery.

Question: What kind of molecular basis required for cancer recovery by Huaier ?

Hypothesis: It should be a system to satisfy various phases clinical significance of anti-cancer effects

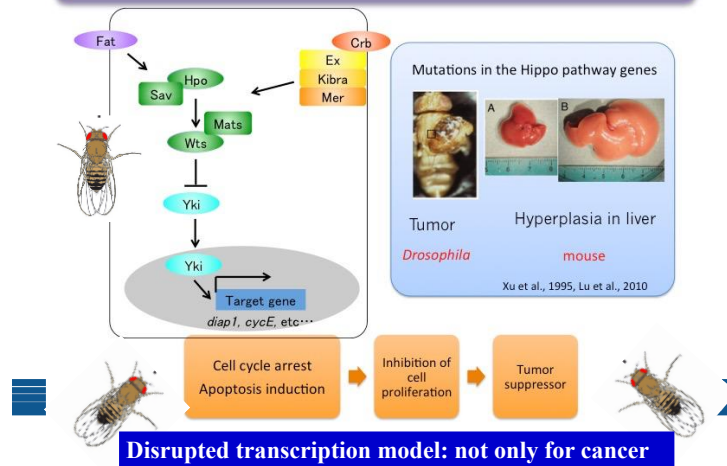
Something to rescue integrated signal networks in the cell

Such as Hippo Signaling Pathway !!



In 2017, we decided to investigate the molecular basis of Huaier effects. Since Huaier has a variety of efficacy not only on cancer, but also on many disorders, we should make a hypothesis to begin with. As shown in the slide, we set Hippo Signaling Pathway rescue function to begin with.

Verification of *Drosophila* model for the experimental design

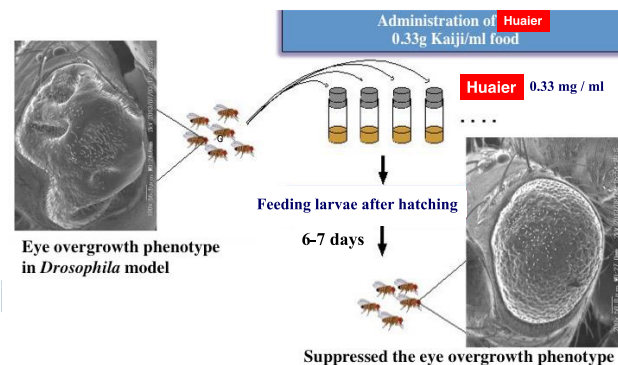


Disrupted transcription model: not only for cancer

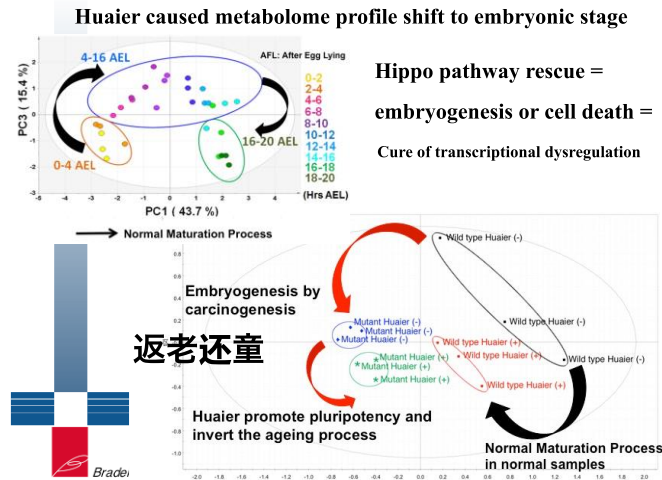
Hippo signaling pathway was first found in *Drosophila* flies, so we started our experiments with transgenic Hippo mutant flies treatment. These mutants are hepatoma model, too. All the genomes were completely analysed. We are very pleased to introduce a simple and complete success to prove our hypothesis.

Simple proof of Hypothesis

Cure of Cancer identified using transgenic *Drosophila* fly model with disrupted function in Hippo signaling pathway.

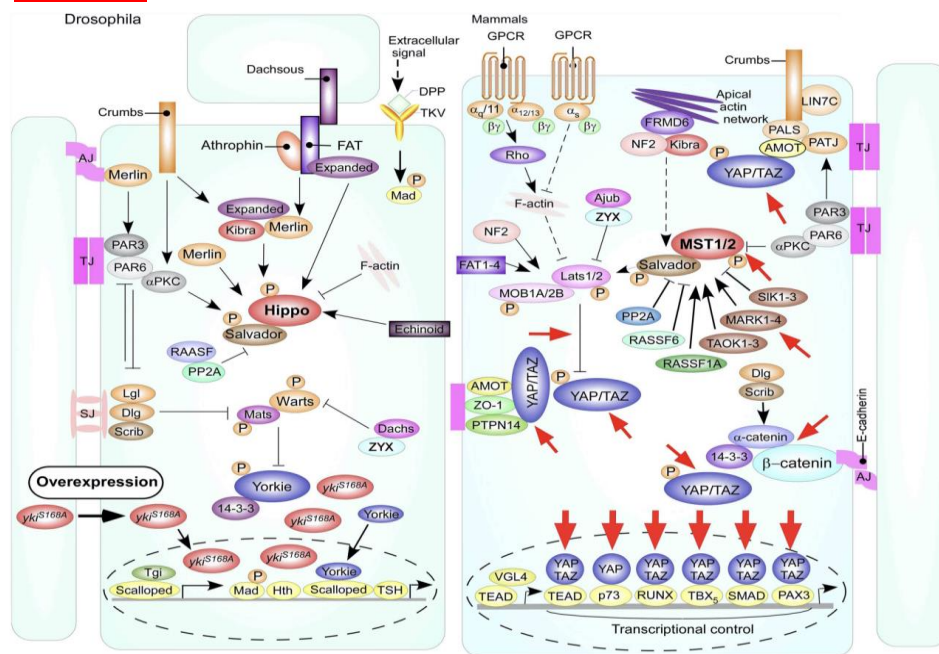


Cancer progression is expressed as malformation and disruption in *Drosophila* eye discs, easy to find and count. Hatched Hippo mutant larvae was raised with Huaier-containing food, resulted in the cures cancer within one week. In this experiment, we could also confirm that dose-dependent action of Huaier, with no toxicity nor significant side effects.



One more advantage of *Drosophila* model is that we can know the metabolome profile of drosophila specimens used in the experiments, the small molecule composition. Usual growth makes the composition move to clock-wise rotation, whereas cancer mutants has already rotated to counter-clockwise position. Huaier treatment made stronger shift to the counter clockwise rotation, shifted to the time zero of life, to the embryonic stage. I should emphasize that, just noted as a specific character of Hippo signaling pathway, the rescued function of Hippo is most effective and functional in iPS/ES cells. The rescue of Hippo pathway by Huaier rewinds biological time to the early embryonic stage judging from the nutrition compositions.

Huaier rescues disrupted function of Hippo signaling pathway

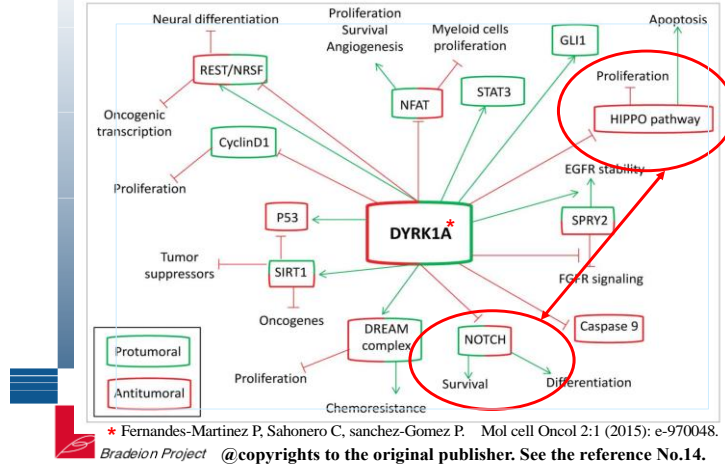


From the review article by Mo, JS, Park JW, Guan, KL (*EMBO Rep* 25: 642-656).

→ Huaier effects on the rescue of function

The schematic figure of Huaier rescue points on disrupted Hippo signaling pathway control. Red arrows show the point of Huaier action.

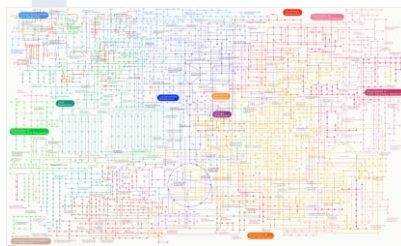
Predicated Huaier effects with a strong similarity to DYRK1A: dual-specificity tyrosine-regulated kinase 1A)



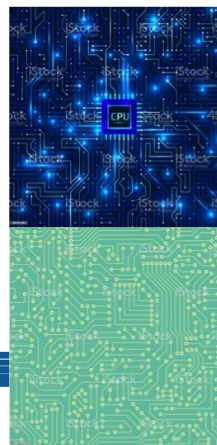
To start with Hippo signaling pathway rescue, multiple functions are designated to be related to cell proliferation, apoptosis, immunological response, and neural differentiation. Just like tyrosine kinase DYRK1A reported before.

Strong similarity of intracellular signal transfer and IC chart

A. Intra-Cellular multi-signal trafficking on metabolic pathways

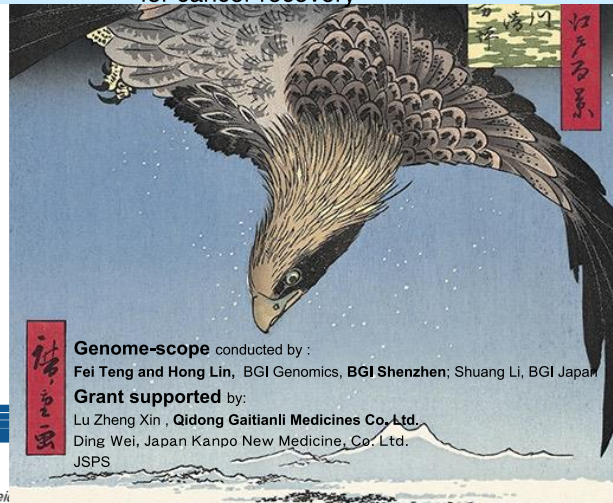


B. Integrated Circuit (IC) chart



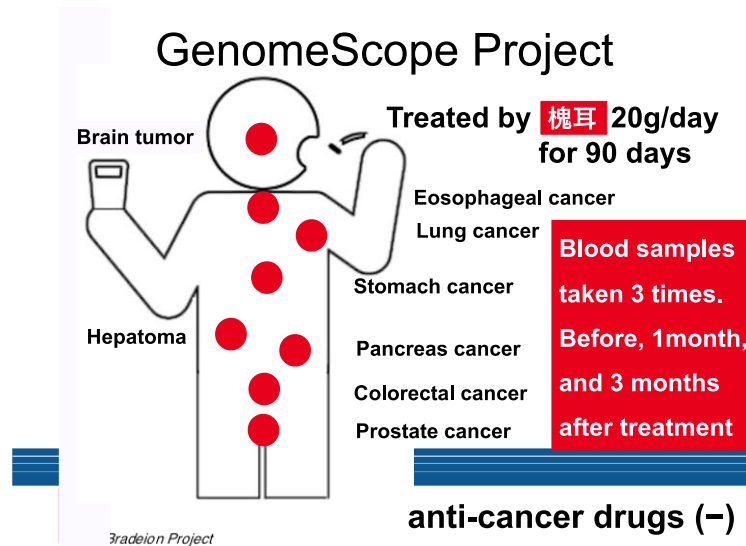
Here is shown schematic figure of intra-cellular signaling cascades. Please note the strong similarity with integrated circuit in your smartphone. This means none of simple stimulus stands alone. Every signal relates each other, and spreads to every direction

Sky-high View of Genomic Landscape for cancer recovery

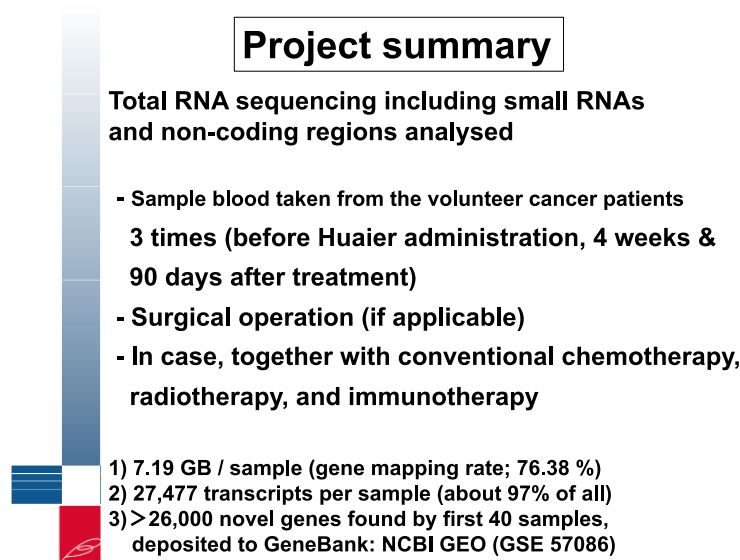


Materials and Methods:

From here, the genome scope results explaining how and what required for cancer recovery. We are watching amazing aspects of genomic capability, flexibility, and possibility in human life, please have a sky-high view to see the genome scape. Never trapped in a trifle name of each factor.

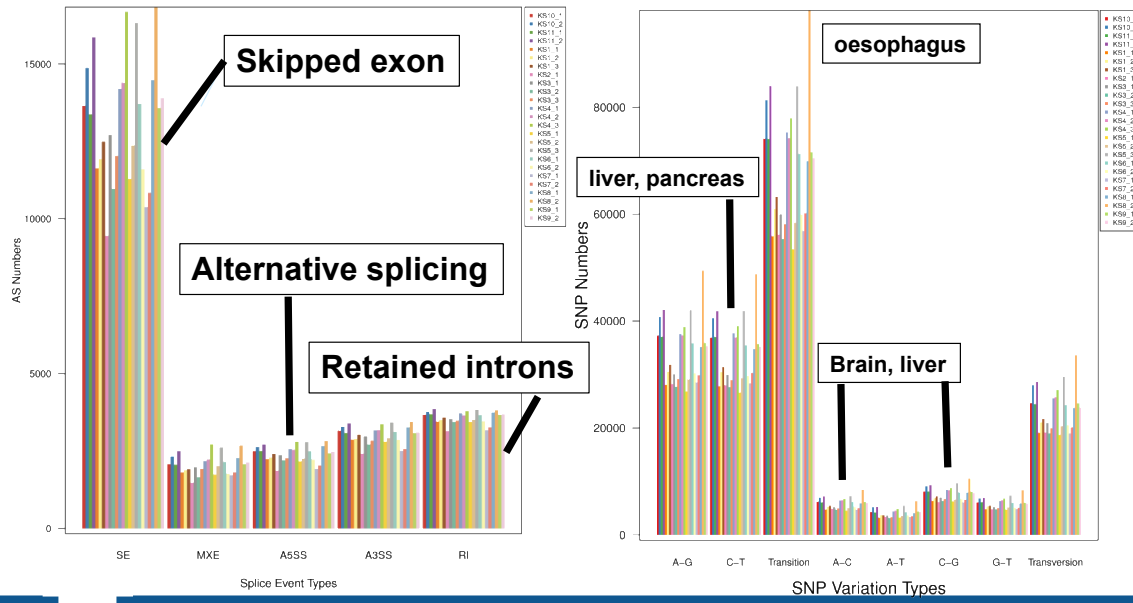


We have performed systematic transcriptome analysis by total mRNA and small non-coding RNA sequencing before and after the Huaier



Project summary. Patients may undergo the surgical dissection during research period. Basically, no other treatment during this clinical research, only one exception of pancreatic cancer shown before.

Extreme SNP variance by Huaier uptake

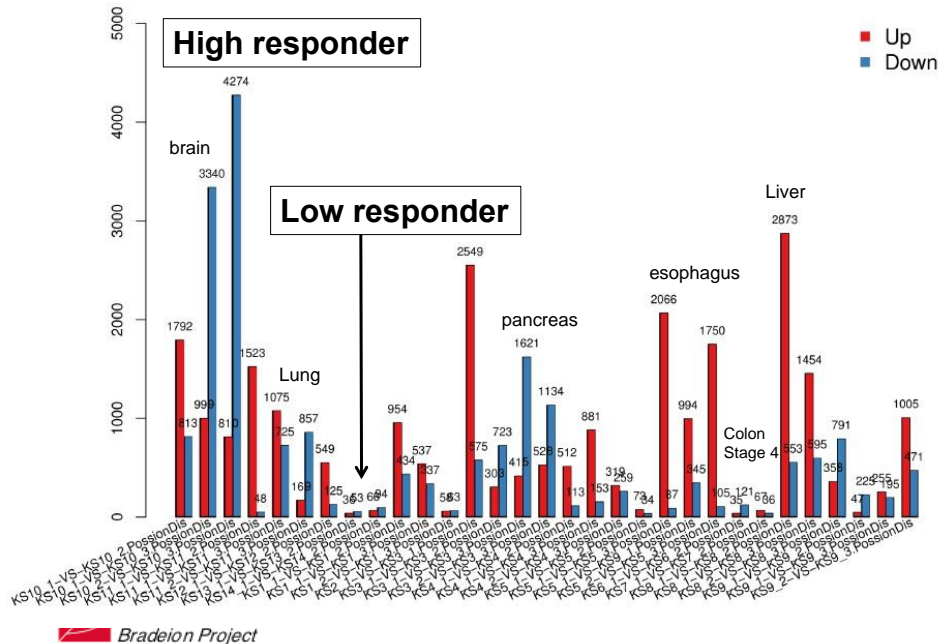


Bradeion Project

Total number of SNP variance by Huaier administration: 8,503,297
 Average : 92,427 (48, 994~146,102)
 Average number of normal healthy control: 22,688

Results and Discussion: I introduce the striking results according to the process of translation and transcription. First, RNA editing events. We happened to identify enormous amount of SNP variant types from 92 sample analyses, and 92,427 SNP per sample, whereas 22,688 in total among normal healthy individuals. Please note the extremely high numbers of mutated sites among all the expressed genes, most commonly found alteration is the skipping exons, different from the predicted pattern of alternative splicing. Huaier caused over thousands and thousands of mutations.

Statistic of Differently Expressed Genes



The slide shows a comparison of up- and down-regulated transcribed genes transcriptomes before and after Huaier administration. Not only by quality, quantity of expressed genes was drastically changed. In hepatoma patient, up to 85% of the total was upregulated within 30 days. Then observed down-regulation and gene-silencing, until the end of research period. The typical time-course of changes were detected in brain tumor and Hepatoma patients.

Quantitative analysis of Up- and Down-regulated differently expressed genes (DEGs) by time course of Huaier administration.

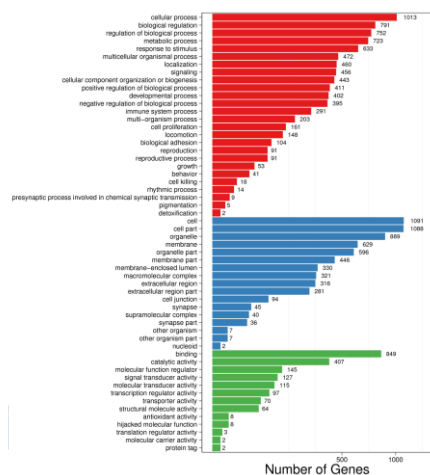
Huaier administration Patient No.	30 days up	30 days down	90 days up	90 days down	6 months up	6 months down	9 months up	9 months down	11 months up	11 months down	1 year up	1 year down	14 months up	14 months down	1.5 year up	1.5 year down	Total Up	Total down
1	954	434	58	63													1,012	497
2	diseased after 1st sampling																	
3	303	723	528	1,134													831	1,857
4	512	113	319	259													831	372
5	67	28	1,750	105					2,351	3,351			3,468*	2,847	147	560	7,783	6,891
6	35	121															35	121
7	67	36															67	36
8	2,877	554	358	791	720	850	3,330*	3,505					3,533	2,891			10,818	8,591
9	47	225	1,005	471													1,052	696
10	1,799	812	810	4,247			5,671*	2,477					3,540	3,439	215	200	12,035	11,175
11	1,523	48	169	857													1,692	905
12	549	125	1,826*	353													2,375	478
13	36	53	1,119	505													1,862	558
14	66	94	1,685	1,178													1,751	1,272
15	1,455	1,141	60	47													1,515	1,188
16	1,166	736	35	186													1,201	922
17	313	239	140	442													453	681
18	664	498	62	183													726	681
19	1,580	823	26	186													1,606	1,009
20	21	30	3,746	3,103													3,767	3,133
21	204	82	1,424	2,746					3,094*	2,037	68	71	97	196			4,887	5,132
22	830	1,557	89	78													919	1,635
24	2,615	3,031															2,615	3,031
25	68	71	97	196													165	267
26	534	2,430	2,235	460													2,769	2,890
27	147	281	215	56													2,769	2,890
28	39	46	103	73													2,769	2,890
29	224	330	319	120													2,769	2,890
30	157	1,548															2,769	2,890
31	1,251	351															1,251	351
Average																	2,589	2,273
Max																	12,035	11,175
Mini																	35	36



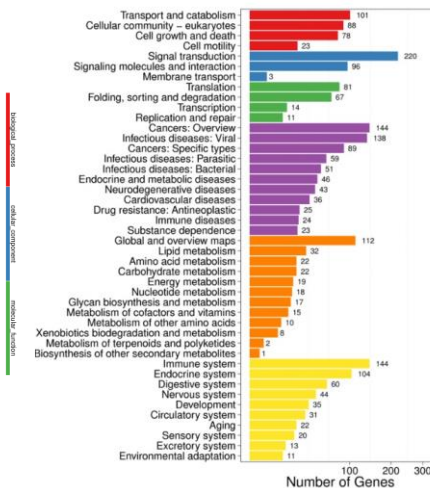
Alteration of 10 to 50 % of all the transcripts

The slide shows the real numbers of alterations in transcribed genes. Let's have a closer look into the numbers of the functional alterations induced by Huaier treatment. Please note the massive quantity changes found in each patient as noted by the previous slide.

Numbers of gene variants by genetic functions



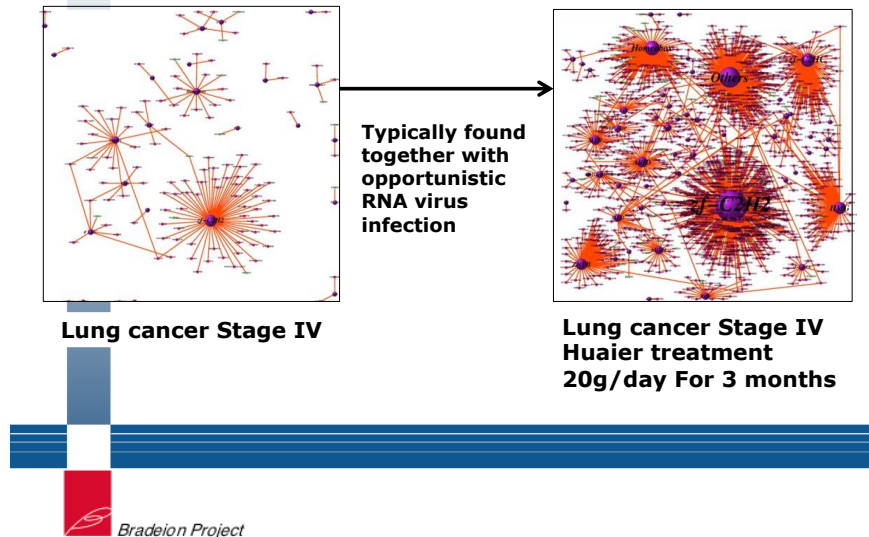
Numbers of gene variants by pathway classification



For the rescue of dysfunction in each signaling cascade, chiefly by ageing, the transcriptional factors, written in red letters, contributed most. As shown in the slide, the alteration of transcriptional factors changed at most for the rescue of every biological function.

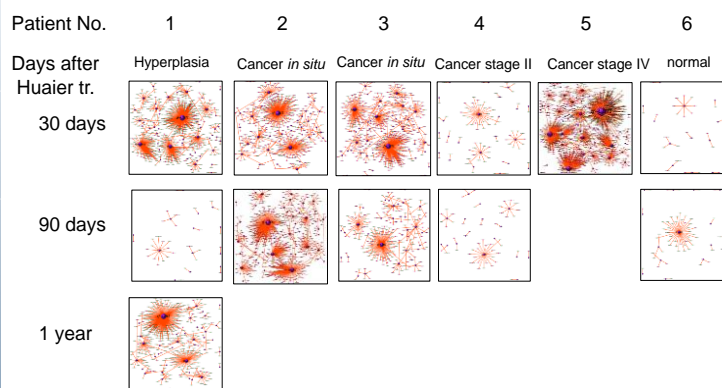
Here we provide the typical answer to the question using the data obtained why and how Huaier is so effective. Huaier causes surprising enhancement of gene function in almost all known transcriptional factors, responsible for the correction of transcriptional misregulation. Thus, Huaier can modify and rescue the function of integrated intra- inter- signaling pathways. These alterations in transcriptional factors can be detected in every cancer listed here.

Over-stimulation of iPS/ES production *in vivo*



Schematic figure of transcription factor (TF)-differentially expressed genes (DEG) network indicated unbelievable level of gene explosion, we call this “super-nova”. The original gene functions of this patients were strongly inhibited and down-regulated by the long course of chemotherapy with molecular targeting drugs. These changes will be silenced after the cure of cancer by Huaier treatment. The drastic changes of altered transcribed genes were united by many transcription factors. In this slide, the total changes of transcriptional factor and differentially expressed genes network showed galaxy structure like volcano eruption. I have to note that these data can not be obtained by experiments using *in vitro* cultured cells, artificially. Many researchers tried, and all the cells dead.

TF-DEG network comparison before and after Huaier administration



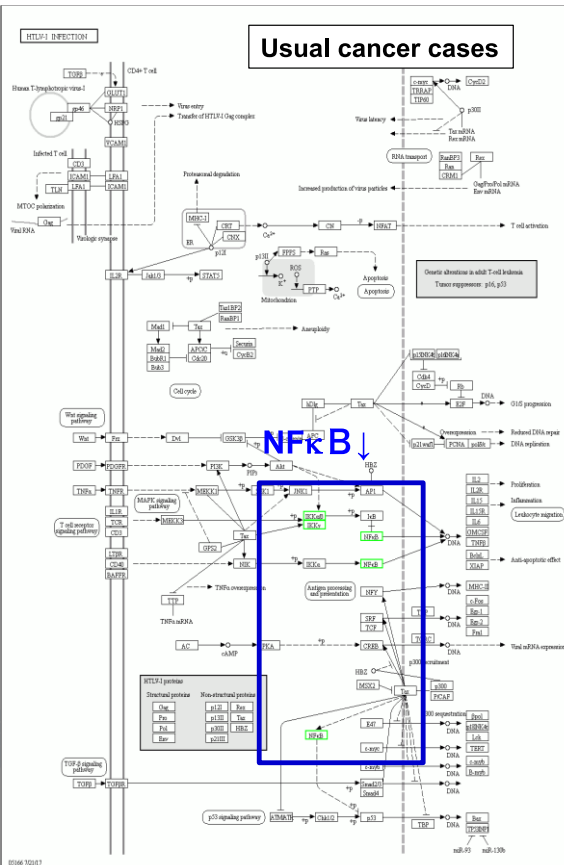
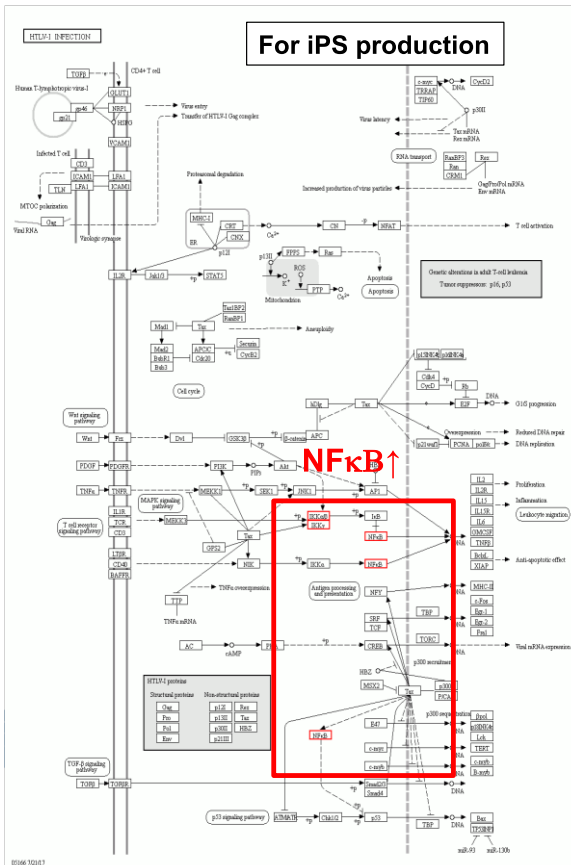
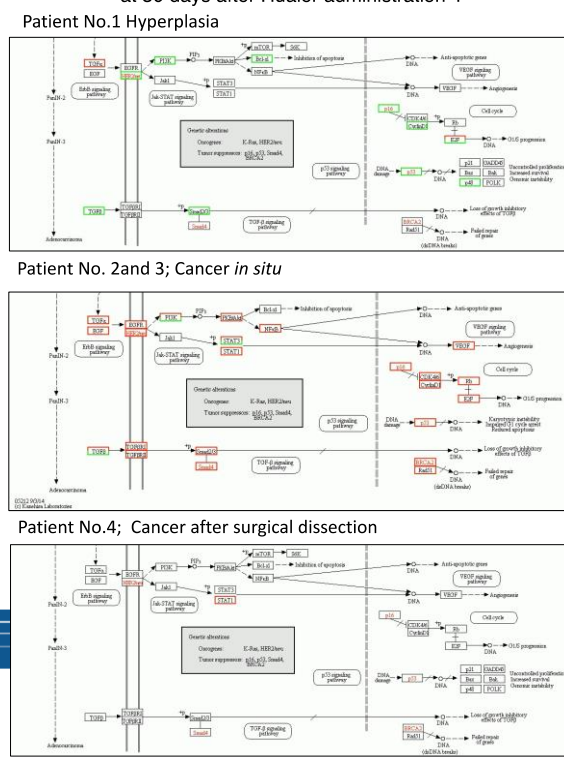
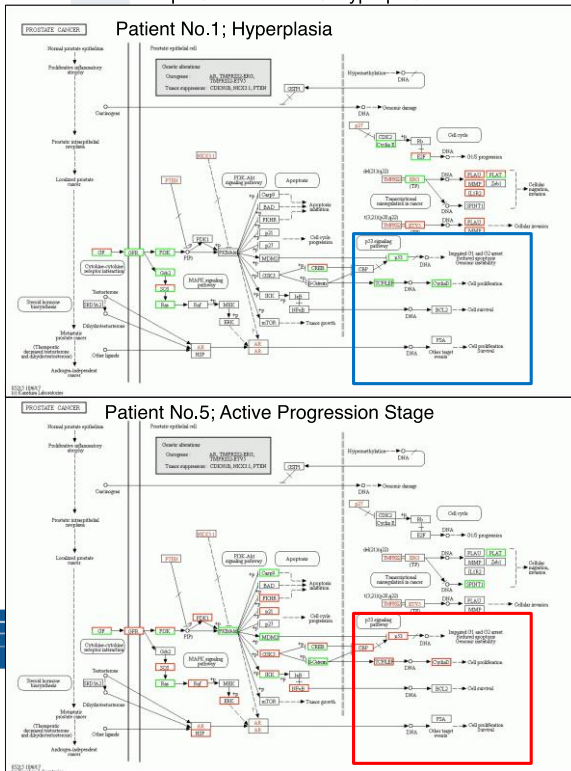
TF: transcription factor, DEG: differentially expressed genes

The slide shows the examples observed in prostate cancer patients.

KEGG analysis for DEG alteration in prostate cancer

Comparison at 30 days after Huaier administration
In prostate cancer vs. hyperplasia

Comparison of TGFβ1, NFκB and BRCA2
at 30 days after Huaier administration-1

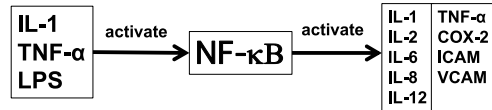


For easy understanding of the major factors for human life, here introduced nuclear factor kappa B to decide a fate of cancer recovery

or more progression in prostate cancer.

NF-κB (nuclear factor-kappa-b)

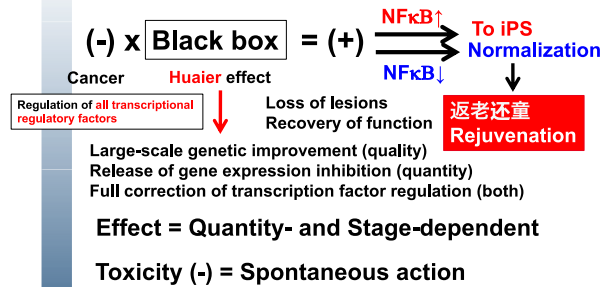
- transcription factor (protein complex, D Baltimore, 1986)
- binds to κchain of immunoglobulin
- originally found specific to B cells, now known as commonly expressed in various mammalian cells
- causes apoptosis, cancer, collagen diseases, allergy and inflammatory diseases, opportunistic infections such as CMV, HTLV)



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Decrease of this factor expression level inhibits cell proliferation, and increase promotes iPS/ES production. Nuclear factor kappa B was first found in 1986 by Dr. Baltimore, and one of the most intensively investigated key molecule to health control. It is important to keep the normal function of NF kappa-B function, not only for immunoregulation, but also for every situation in chronic intrinsic diseases, including cancer, collagen diseases, and other allergic disorders.

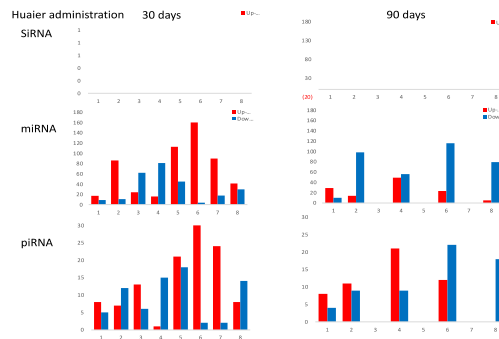
Theoretical mechanism of health recovery



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No compounds or anti-cancer drugs have been reported to evoke the similar drastic changes before, never the less within a short period of time (90 days at most), especially with no toxicity and side effects. I emphasize that the rescue effects ended up with gene silencing, massive suppression of gene expression such as NFκB. The patient has been long treated with strong anti-cancer drug (= significant shut down of gene function). The explosive increase of quantitative and qualitative transcriptomes was occurred within 3 months' Huaier treatment by 20g to 60g per day, seemed to be resulted in natural selection of iPS cells *in vivo*, with abundant c-myc and Oct3/4 gene expression, and with normal level Sox2 and Kit4, together with severe opportunistic HTLV-1 infection.

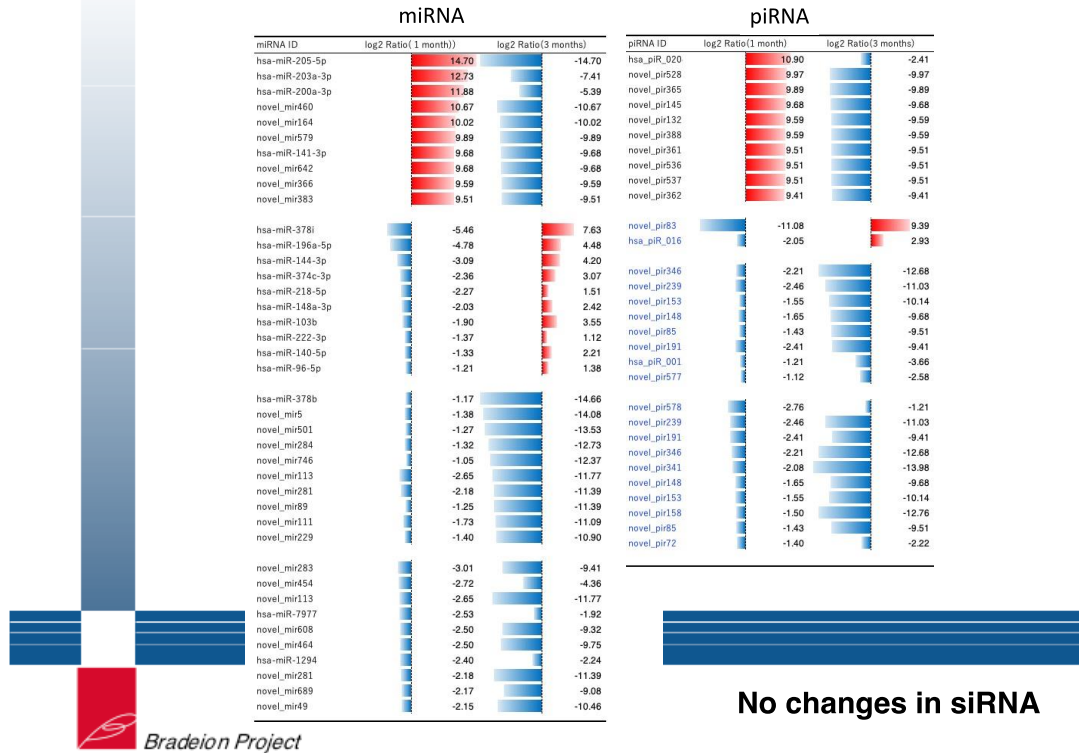
Small nuclear RNA changes in various cancer patients



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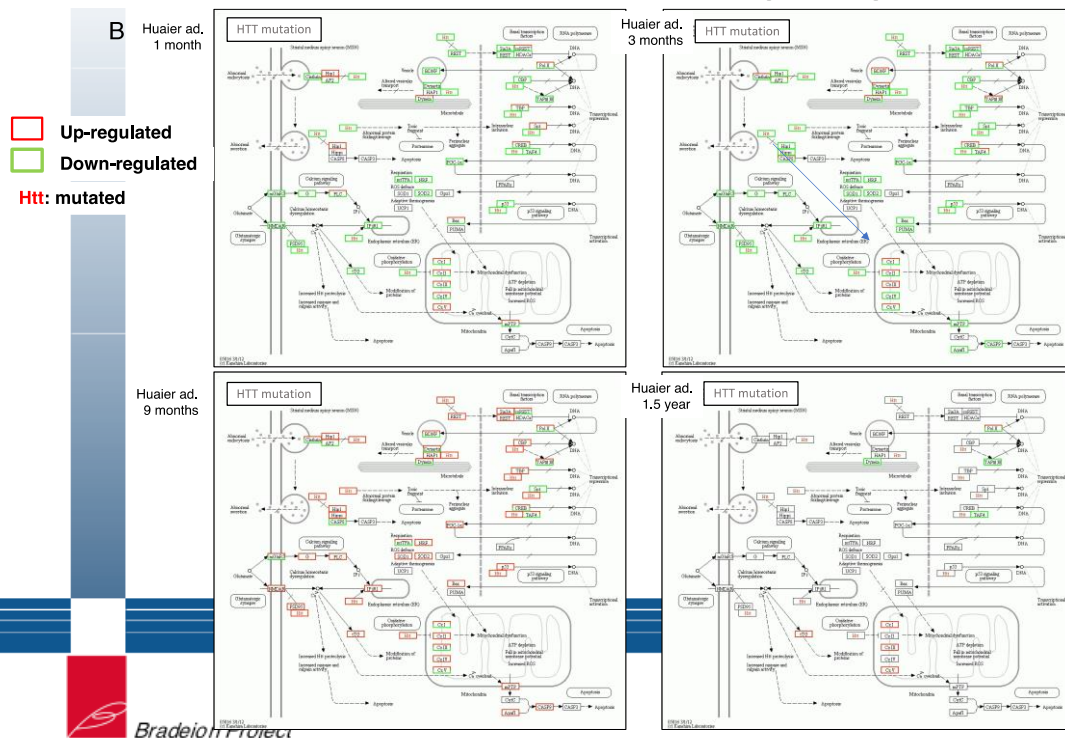
Let’s have a closer look into another influencers of the transcription control. Small nuclear RNAs. Beyond our expectations, many novel factors are found and deposited to GeneBank. So, most of their functionals are still unknown. This slide show the discovered novel factor level of each patient.

Small nuclear RNA changes in the brain tumor patient

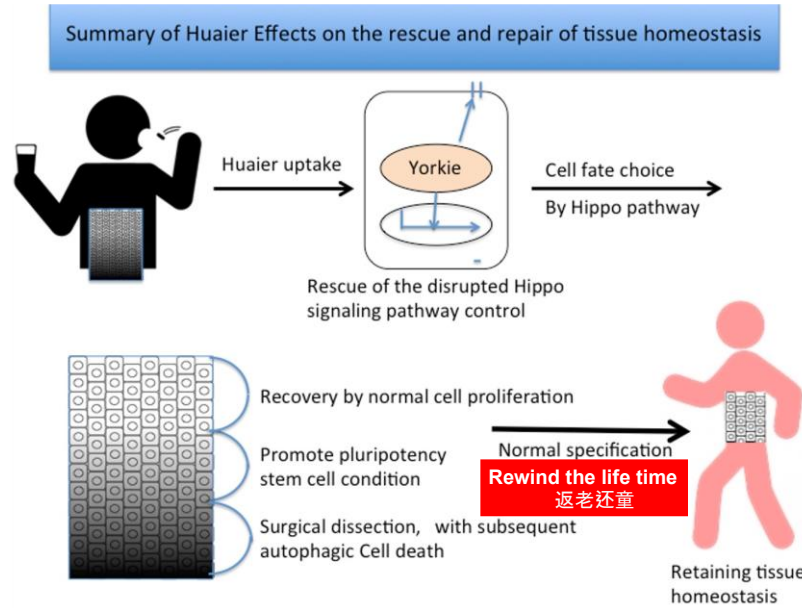


For example, the quantitative changes of each factor are shown. The quantity was changed according to the duration of Huaier treatment. After surgical dissection, quantity regulation was completely reversed in some factors.

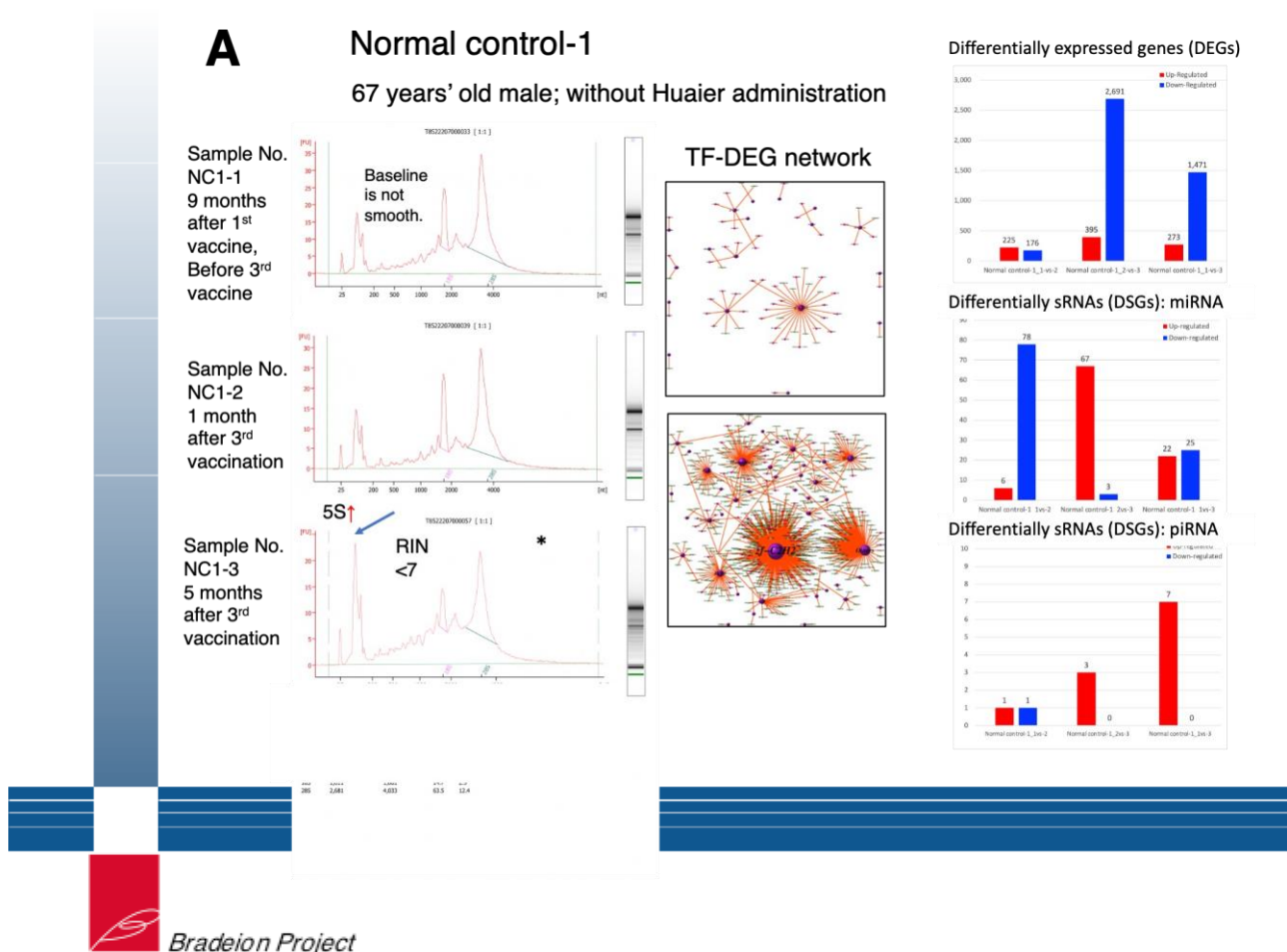
Huaier effects on neural transmission signaling cascade



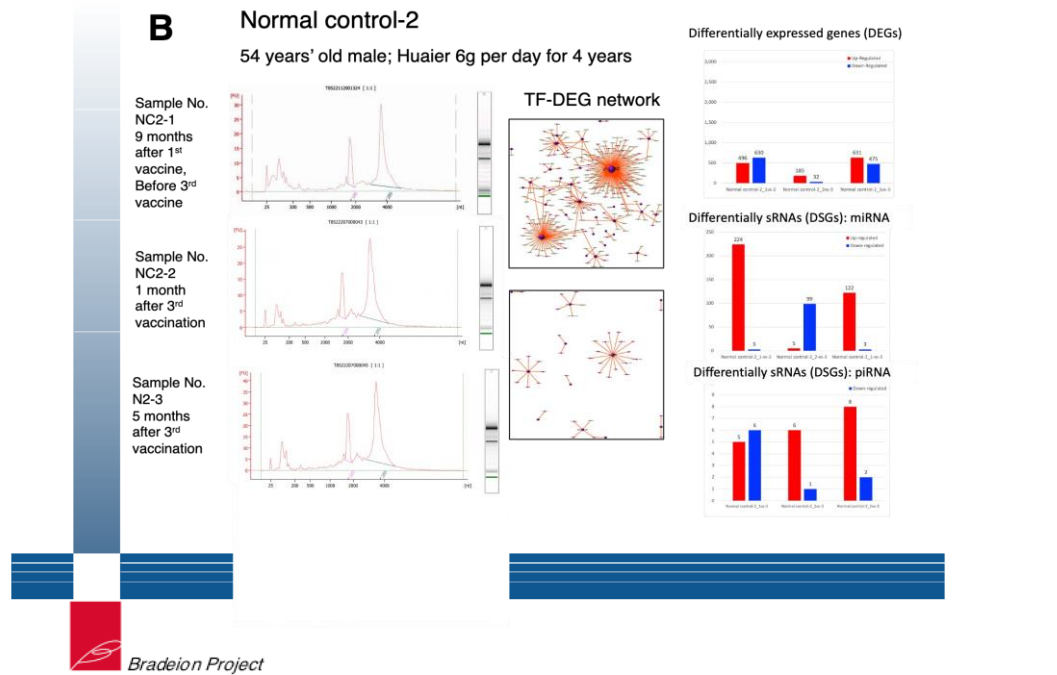
In addition, I have to note that Huaier influences to neural transmission, too. Here showed KEGG panel of Huntington's Disease signaling cascade, but there are more panels on Alzheimer's, Amyotrophic lateral sclerosis, and psychological disorders as Depression.



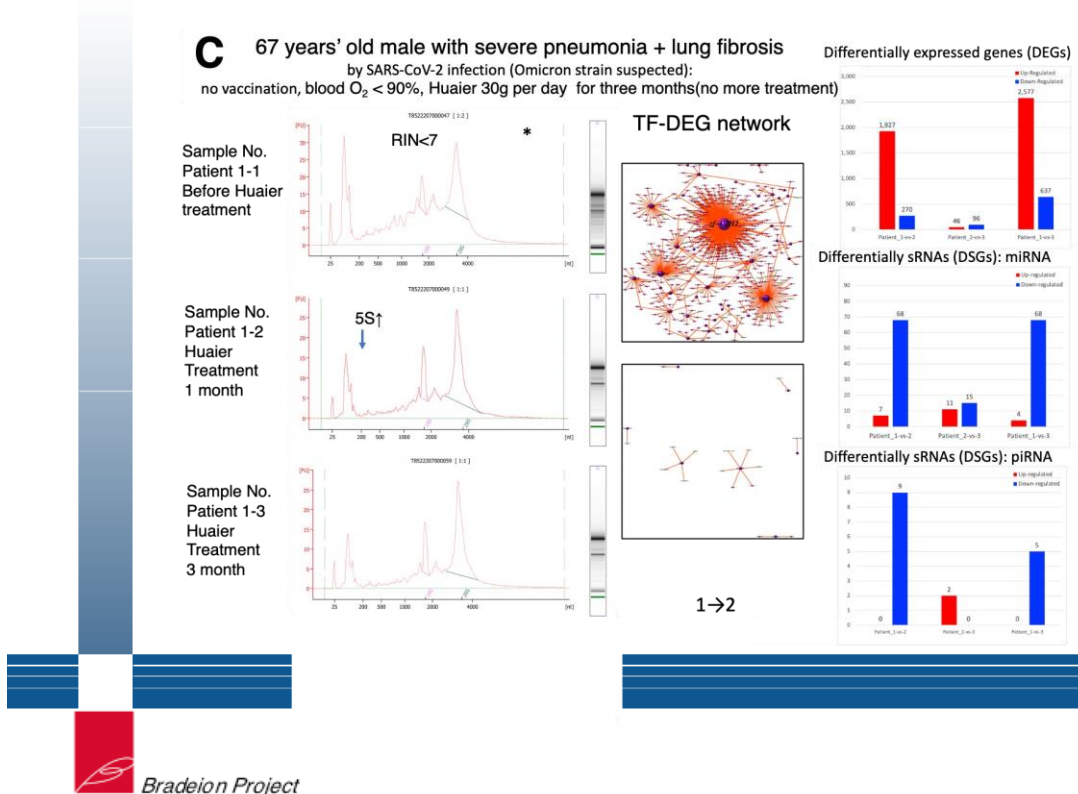
Huaier rescues the disrupted Hippo pathway, which decides cell fate, to initiate the normal specification of the damaged tissue cells, to recover the homeostasis of renewed tissues. Huaier itself has a function to kill cancer cells, but surgical dissection is recommended if applicable. Huaier-uptake initiated cell fate shift to embryogenesis, which was typically indicated by the metabolome profile.



Ribosomal structures by HPLC analysis (left column), with TF-DEG network (middle column). The time of sampling, and Pfizer-BioNTech vaccinations (panel A. normal control 1; panel B. normal control 2; panel c for patient data) are indicated on the left side of each panel. The red and green dots in the TF-DEG network represent the up-regulated and down-regulated DEGs, respectively. The purple ball represents a transcription factor, and the greater the node is, the more DEGs the transcription factor regulates. In the right column of each panel, a comparison of the numbers of differentially expressed genes (DEGs) was placed according to the time course of Pfizer-BioNTech vaccination; red bars represent up-regulated molecules, and blue bars represent down-regulated molecules.



Panel B. normal control 2, this 55 years' old surgeon is having 3 grams of uaier daily for 4 years, Panel C for COVID-19 patient data indicated on the side. Chest CT image analysis before (March 15) and after 3 months of 20 grams daily Huaier treatment on the patient (June 28).

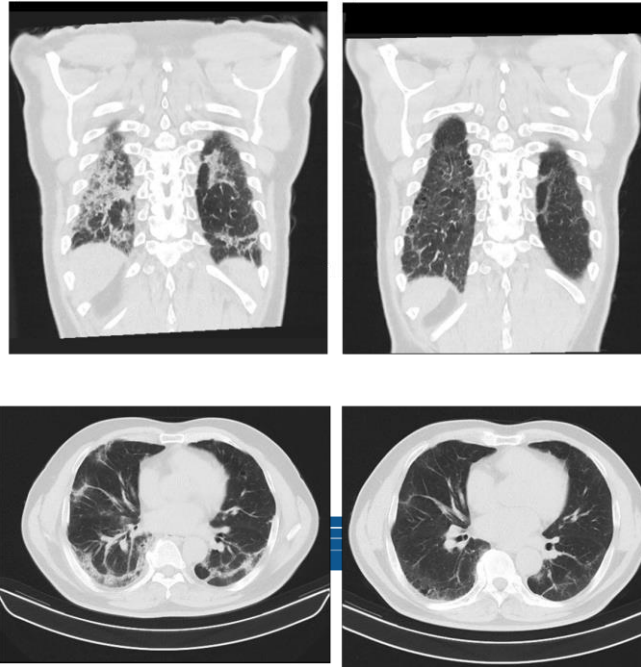


CT image analysis
67 years' old male with severe pneumonia + lung fibrosis

C

Before Huaier treatment
March 15, 2022

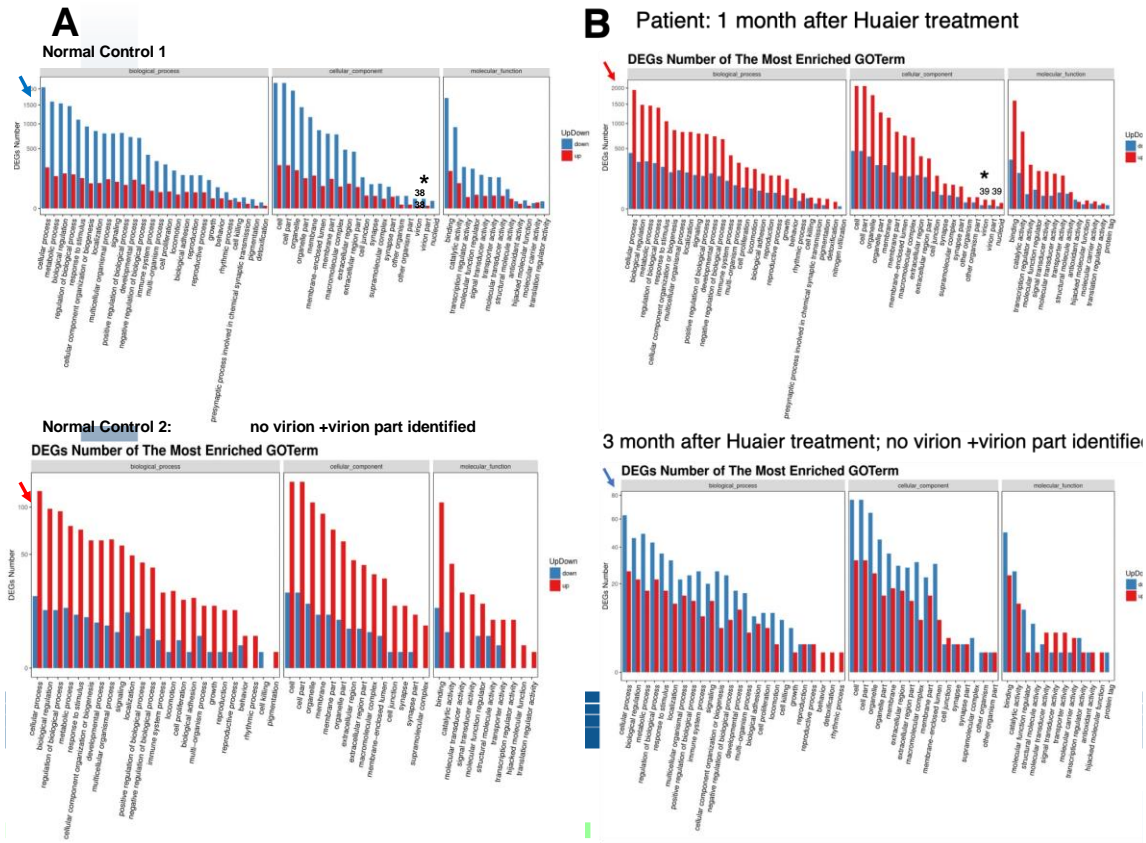
3 months after Huaier treatment
Jun 28, 2022

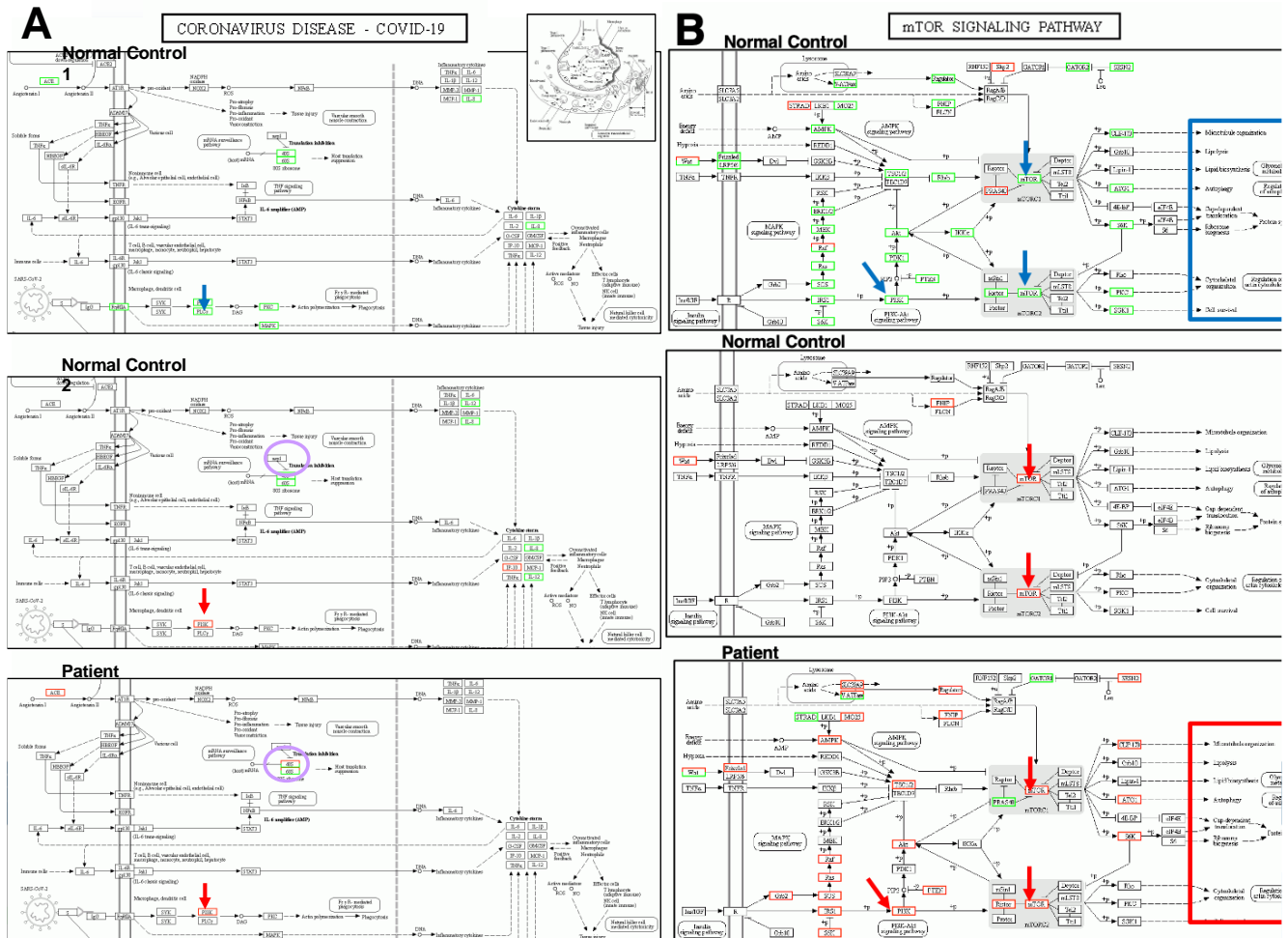


Bradeion P

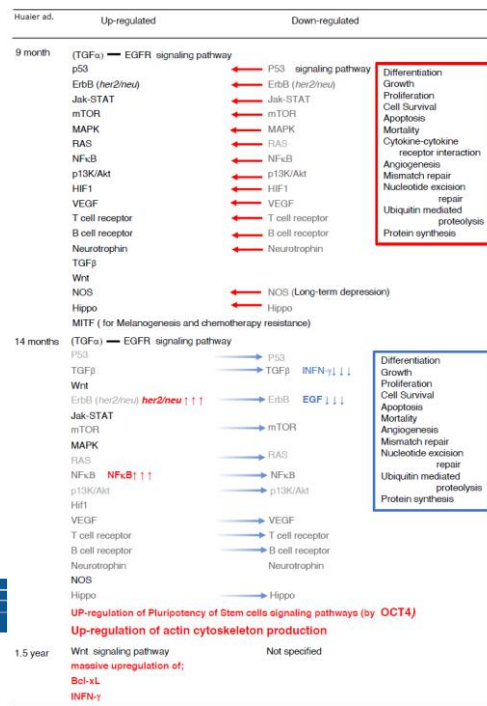
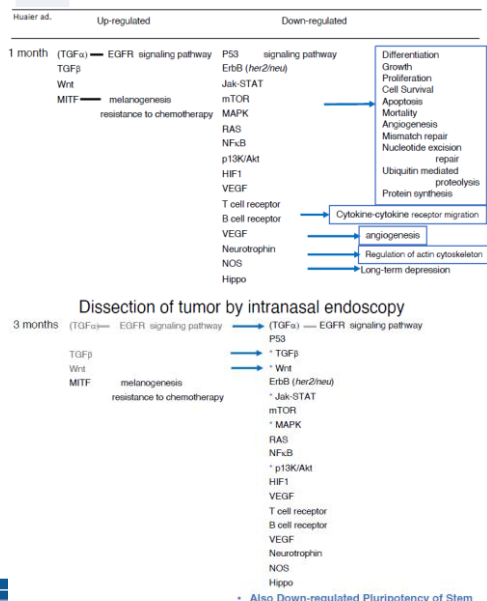
Ribosomal structures by HPLC analysis (left column), with TF-DEG network (middle column), of this patient.

In the next page, we demonstrated virions and virion particles in the vaccinated patient blood specimens after vaccination (Panels A and B) as well as infected specimen (Panel C).





Intracellular signaling cascades rescued by Huaier treatment



Huaier 20g / day for 2 years
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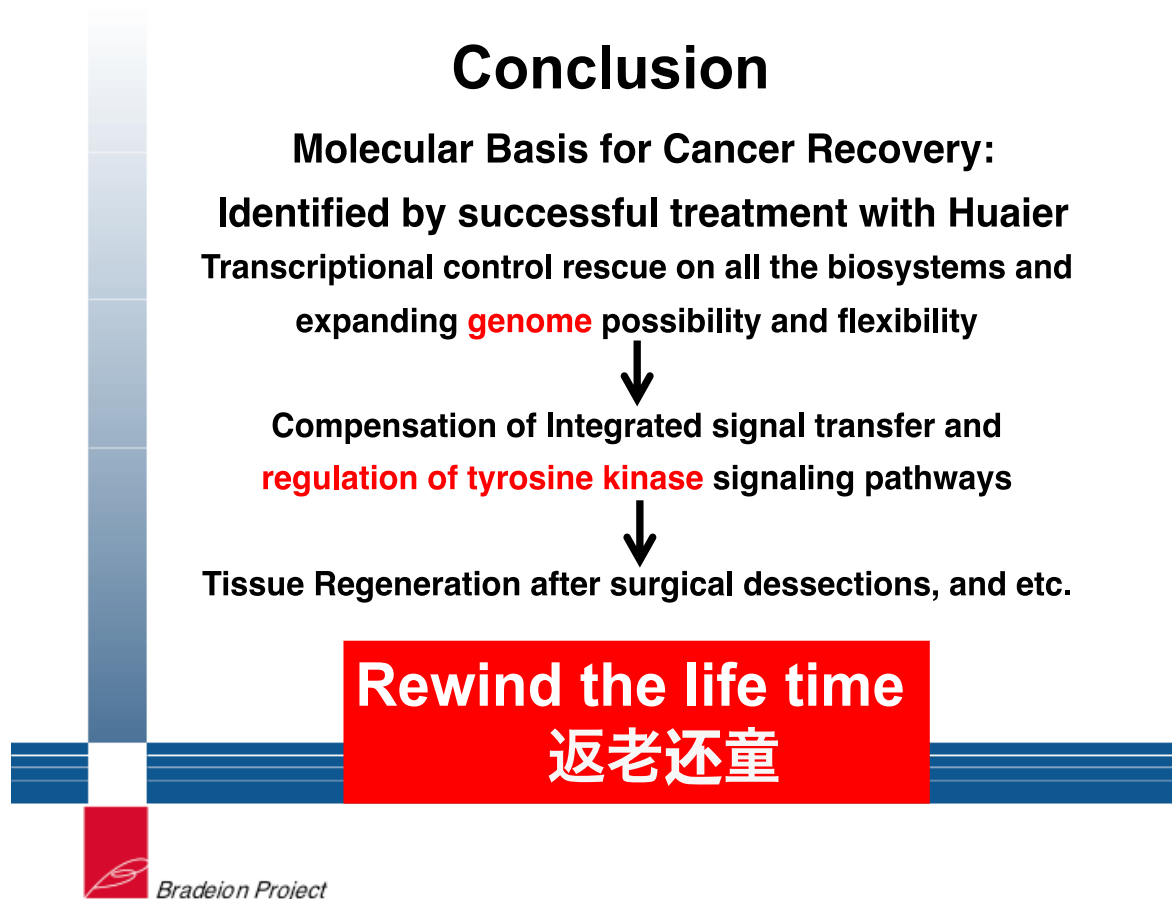
KEGG pathway analysis on COVID-19 panel hsp05171 (Panel A) and transcriptional misregulation and the P13K/AKT signaling pathway Panel B). Huaier administration was applied in the patient and normal control No.2. (5 g/day). Red bars represent up-regulated molecules, and blue bars down-regulated molecules. The figure was chosen at the time of the highest transcription factor-DEG network flexibility in each patient among serial analyses over a long time course of treatment.

Here shows the representative signaling pathways function rescued by Huaier treatment. The patient treated only by 20 grams of Huaier every day for two years. You can see the wide variety of cellular function was rescued, and that by the time course of Huaier treatment.

Conclusion:

Carcinogenesis is a long process caused by step-by-step accumulation of genetic mutations and environmental stresses. But as shown in this presentation, the process of the cancer recovery required drastic alteration on transcribed genes within 4 weeks at first. Please note that what kind of compounds can do this much changes *in vivo*?

Molecular basis of Huaier effects exists in the expansion of genome power itself, and the rescue of transcriptional dysregulation not only in Hippo signaling pathway, but also all the integrated signal transduction systems, especially relating to tyrosine kinase pathways. No other medicine has not yet been reported to evoke the equivalent changes. These changes occurred spontaneously in the patient, with no toxicity nor side effect. In addition, significant NF- κ B increase and its signaling pathway seemed to be responsible for the natural selection and production of iPS/ES cells, with subsequent differentiation to normal cells.



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Author contributions:

M. T., F.T., H. L., designed the study from the clinical observation of the cancer patients with Huaier treatment (as a complementally therapy), and managed the sampling and clinical assessment of the

patient volunteers, statistically analyzed the data, and drafted the manuscript. F. T., X. Z., H. L. Z. L., managed total RNA and small nuclear RNA sequencing and conducted systematic analysis of the data. S. S., T. S., and Y. M., contributed clinical diagnosis and treatment of the patients, together with the assessment of QOL and the effects of Huaier administration, Z. L., D. W., contributed to the provision of Huaier granules and clinical evaluation of the data, especially focused on Immunological evaluation.

Competing interests:

The authors declare no competing interests.

Data availability:

The complete sequencing data of the cases have been deposited to NCBI database, and the clinical outcomes of these cases are not publicly available for data privacy but are available from Dr. Manami Tanaka (e-mail: tubu0125@gmail.com, manami-tanaka@bradeion.com) upon request for research collaboration. The timeframe for response to data access requests is 30 days. There are no restrictions on the reuse of data. In addition, the raw data of the longitudinal cohort and healthy individuals analyzed in this study were available at GEO with identifiers of NCBI GEO (GSE157086).

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Also see.

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