Introducing Omnitura Therapeutics

February 10, 2016

Prepared for Merck
Internal Use Only

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Omnitura:
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Omnitura Therapeutics

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Purpose of Meeting With Merck

- **Omnitura introduce Aneustat™ the ubiquitous cancer therapy which is ready for licensing and joint phase IIb development – invite Merck to consider take lead to accelerate Aneustat™ to maximum number of patients with unmet need**
- **Introducing Aneustat™ synergistic combination with other I.O. drugs – invite Merck for clinical collaboration**
- **Introduce Genyous for autoimmune and neurodegenerative diseases) – invite Merck for pre-clinical collaboration**

Aneustat™ Potential Ubiquitous Application to Intercept, Treat, and Prevent Cancer and Co-Existing Diseases to Reduce Disease Incidence and Healthcare Cost

Clinical Strategy	Cancer Interception		Treat/Prevent Metastasis Prevent Recurrence			
Target Organ	Chronic Benign Diseases ⇏	Pre-Cancerous Condition ⇏	Early Stage Cancer **X**	Late Stage Cancer **X** in combination with other standard of care		
Prostate	**X** BPH Prostatitis	**X** PIN/PIA	Active Surveillance	**X** Standard of care for Chemo-Naïve mCRPC/adjuvant	Standard of Care for Chemo or AR refractory mCRPC	**X** Treatment for triple-refractory mCRPC
Breast	**X** Chronic Inflammation (dense breasts)	**X** Atypical DH BRCA1&2 Family History	Post initial curative surgery DCIS	**X** Standard of care for Chemo-Naïve/adjuvant	Standard of care for previously treated	**X** Standard of care for refractory
Pancreas	**X** Diabetes And Pancreatitis	**X** Family history and predictive genetics IPMN	progression after initial radical surgery	**X** Standard of care for Chemo-Naïve/adjuvant	**X** Standard of care for previously treated	**X** Standard of care for refractory
Lung	**X** COPD	High risk population	**X** Post radical surgery progression	**X** Standard of care for Chemo-Naïve/adjuvant	**X** Standard of care for previously treated	**X** Standard of care for refractory
Colon	**X** IBD	**X** FAP HNPCC	progression after curative surgery for localized disease	**X** Standard of care for Chemo-Naïve/adjuvant	Standard of care for previously treated	**X** Standard of care for refractory
Liver	**X** Cirrhosis	**X** HBV HCV	progression after initial surgical resection	**X** Standard of care for Chemo-Naïve/adjuvant	**X** Standard of care for previously treated	**X** Standard of care for refractory

Initial company clinical development (2015)

R&D partnership projects with cancer foundations (in discussions)

Aneustat™– An Improved Pharmacological Paradigm the SMART Platform for Combination Therapy for Cancer

Systems Diagnosis

Analyze
- Genetic mutation (gene sequencing)
- Chronic disease information status (biomarker)

Characterize
- Validate single function mutation
- Extent of activation of chronic disease engine

Rational Patient Stratification

Stratify patient with:
- Improved and more complete knowledge
- Precision targets identified due to improved signal to noise in all biological pathways

Therapy

Patient Situation		
Pre-Cancer Disease	Early Stage Cancer	Late Stage Cancer
	Local Therapies Surgery or Radiation ±Adjuvant Therapy	Single or Dual Target I.O. or Chemo

+

Aneustat™ (the SMART foundational drug)
- Master controller of all hallmarks of cancer
- Master regulator of the neuroimmune system

SMART™ =
S: Safe/Synergistic
M: Multivalent/Mechanism
A: Adaptive Arsenal
R: Regulation/Restoration to normal
T: Therapy/Treatment

Rationale for Combination of Checkpoint Inhibitors With Aneustat™

1. Checkpoint inhibitors (CPI) would work more effectively if during the course of increased immunological pharmacodynamics, the potentiation of inflammation, unchecked cellular growth and angiogenesis, unresponsiveness to growth regulating factors could be brought controlled.
2. Aneustat™ has been shown in pre-clinical and clinical testing to do the above and create immune equilibrium in a patient.
3. There is a clear rationale for synergy in combinatorial immunotherapy using Aneustat™ as the foundational drug.
4. Omnitura invites partners for R&D collaboration to improve safety and long-term efficacy while minimizing side effects and drug resistance for patients, thus reducing clinical trial risk for single targeted checkpoint inhibitors and next generation targeted immune therapies.

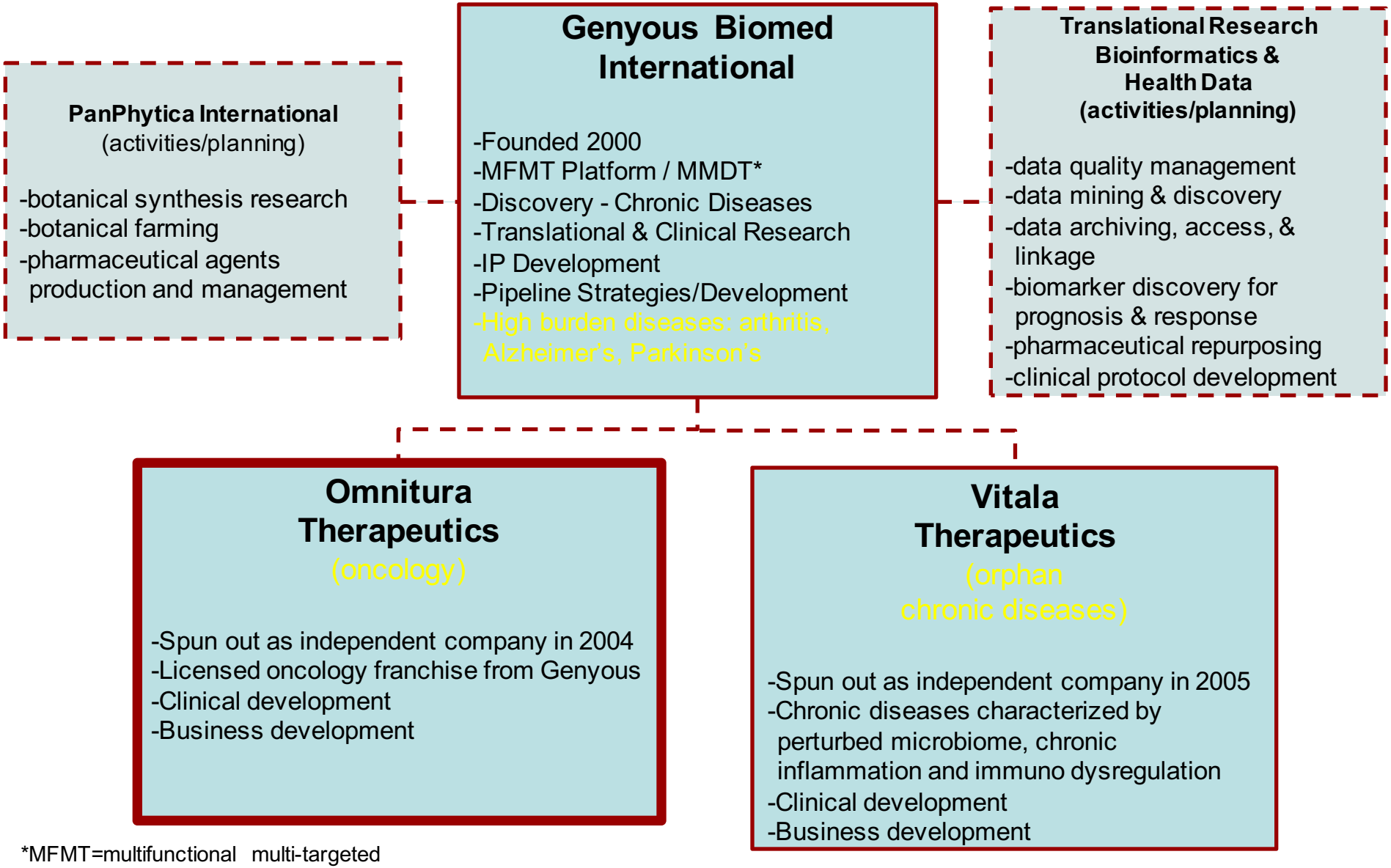
Genyous Biomed has a Platform of Proprietary Multivalent Compounds to Treat Heterogeneous Autoimmune and Neurodegenerative Diseases

- Remove performance barriers of current drugs to intercept, treat, and prevent recurrence of chronic diseases, reduce disease incidence for patients and economic burden for patients and society.
- Increase safety and long-term efficacy to manage specific or co-existing chronic diseases
- Reduce side effects and morbidity and to improve patient productivity
- Create synergistic combinations with current standard of care therapies, legacy drugs, and next generation targeted drugs
- These new combinations could also be patentable block buster drug candidates
- Current opportunities include preclinical to phase II/III clinical development for rheumatoid arthritis, cystic fibrosis, Crohn's disease, multiple sclerosis, chronic fatigue syndrome, autism, Alzheimer's and Parkinson's.
- Genyous Biomed invites collaborators for joint R&D to accelerate a new medical paradigm for treating heterogeneous autoimmune and neurodegenerative diseases.

Introduction of Genyous/Omnitura to Merck
February 2016

- **A group of companies founded in 2000 to create multivalent pharmaceutical products that are safe, effective, and economically sustainable**
- **Our mission is to create a SMART paradigm in pharmaceuticals:**
  - To prevent, intercept, and treat chronic diseases with drugs that are orally delivered, safe, multivalent, and synergistic with standard of care therapies, legacy drugs, and next generation targeted therapies.
  - To minimize disease incidence as well as morbidity and mortality due to chronic diseases—initial focus on cancer
- **We are seeking joint clinical development/marketing partnership for Aneustat™, a potential blockbuster multivalent I-O drug**
- **We are seeking partnership for R&D collaboration for next generation multivalent combination therapy with breakthrough medical value to address broad patient base – for cancer, autoimmune and neurodegenerative diseases**
- **We are seeking investments from companies that share our strategic, product and economic objectives**

Corporate Structure and Development Status

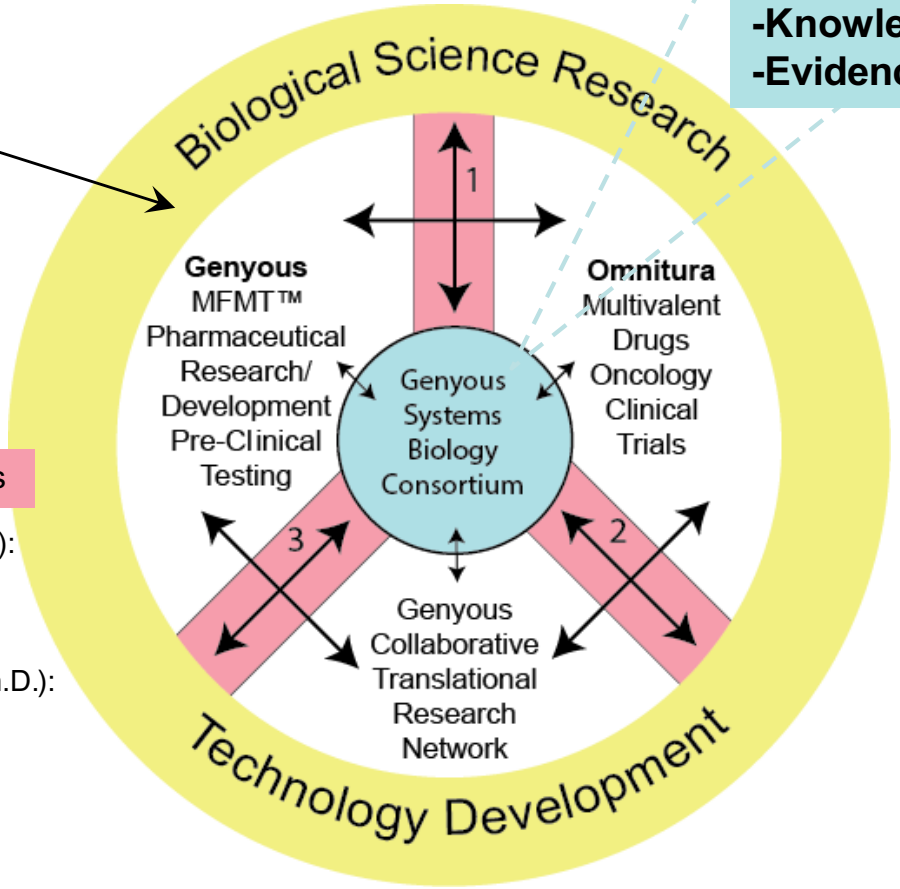


*MFMT=multifunctional multi-targeted
MMDT=multivalent molecularly directed therapy

Collaborative Translational Research
Focus on Systems Biology—Making the Patient Well

Genyous Operating Guidelines:
-Patient wellness driven goals
-Knowledge based decision making
-Evidence based medicine

Existing Scientific Knowledge: Plus new knowledge resulting from $20 billion annual U.S. budget for biotech and disease research in U.S.



Synergize with Pharmaceutical and Diagnostic Industries, Medical Service Community, and Payers to Realize High Value Healthcare for Patients

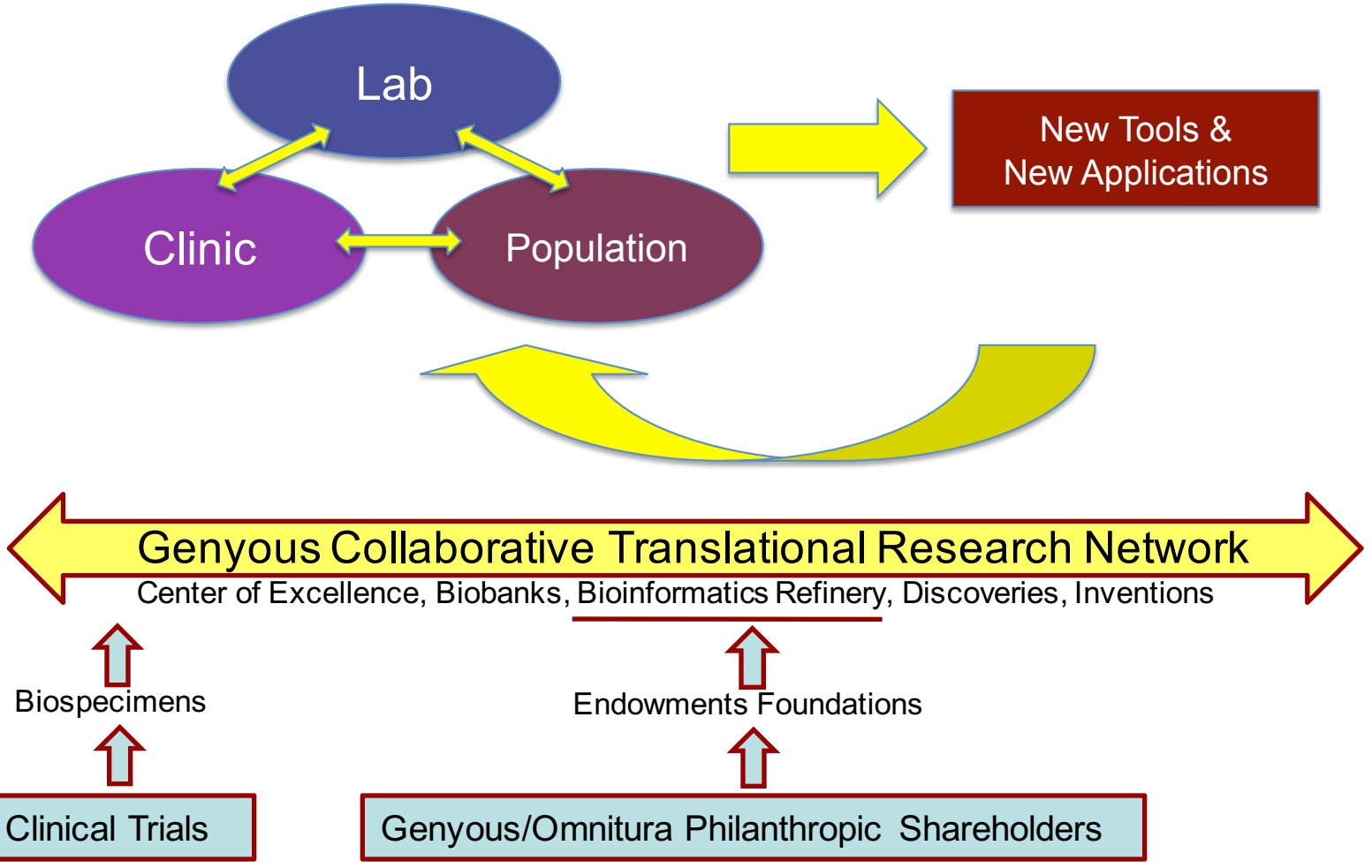
1. Multivalent molecularly directed therapies (MMDT) to manage chronic diseases including cancer, and not to just treat symptoms
2. Form rational combinations of MMDT with standards of care to make breakthrough improvements in safety, efficacy, drug resistance, primary disease recurrence or development of secondary disease
3. Develop patient stratification ensuring that the correct treatments are given to the right patients
4. Exploitation of legacy compounds in existing drug libraries for use in combination with MMDT
5. Disease incidence and economics studies with HMO's and insurance collaborators

Knowledge Acquisition & Synthesis

1. Clinical Scientists-Oncologists (M.D.): trial planning/risk reduction/efficacy/safety/side effects
2. Disease-focused Scientists (M.D./Ph.D.): mechanisms/targets/molecules
3. Systems Biologists
   Biological Researchers (Ph.D.)
   Multifunctional Multitargeted (MFMT)
   Biological researcher:
   -prevention of progression
   -disease modification
   -side effect minimization
   -long term safety
   -tissue regeneration

Genyous Collaborative Translational Research Networks Accelerate Innovations to Benefit Patients and Funding

Objective: To efficiently transform scientific discoveries arising from laboratory, clinical, or population studies into clinical applications to reduce cancer incidence, morbidity and mortality.
(source: Translational Research Working Group, National Cancer Institute, 2007)



Genyous/Omnitura Team & Collaborators

Management Team **10**
research/development
corporate development
marketing
botanical sourcing
drug development
drug manufacturing
program management
finance
legal

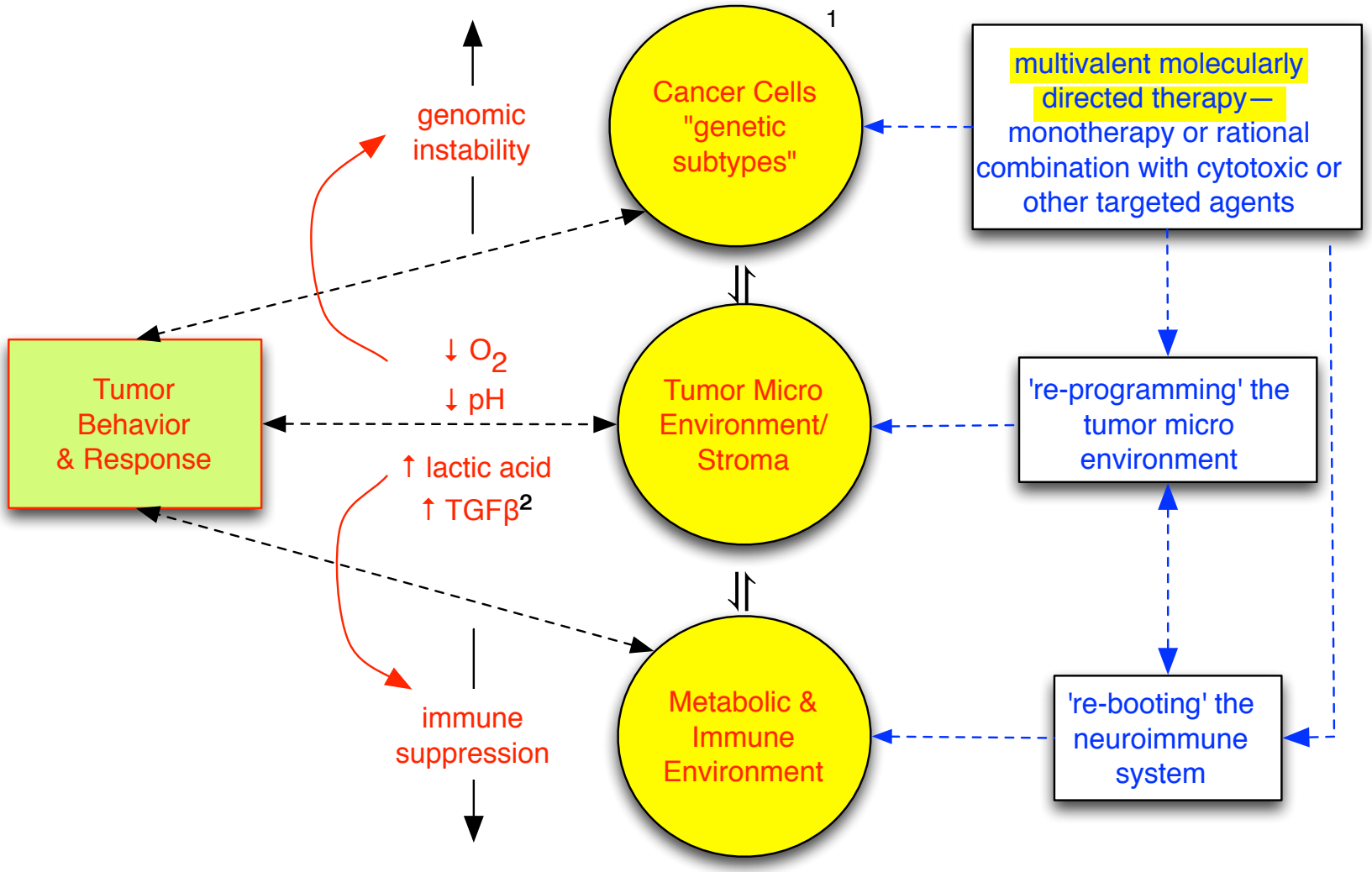
Attorneys **7**
corporate law
intellectual property
regulatory affairs

PhDs **36**
cell biology
systems biology
chemistry
health economics
nutrition
pharmacology
pharmaceutics
immunology
autoimmune
neurology
oncology

MDs **20**
oncology
urology
pulmonology
GI
neurology
pathology

Research Collaborators
BC Cancer Agency
Cedars Sinai
Mount Sinai
Harvard
Johns Hopkins
MD Anderson (UT)
Memorial Sloan Kettering
NCI
Stanford
UBC (Canada)
UC Berkeley
UC Davis
UCLA
UCSB
UCSD
UCSF
University of Arizona
York University (UK)
UT School of Biomedical Informatics (13 research hospitals)
Kaiser Permanente
UnitedHealth

Cancer Biology: Impacts at Cellular, Microenvironment, and Neuroimmune System

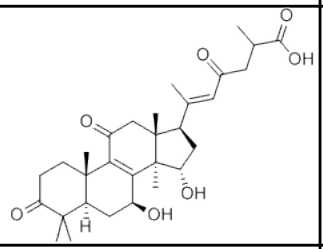
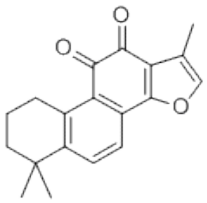
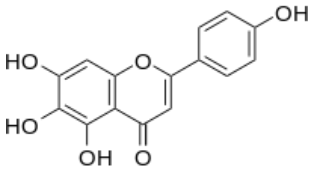
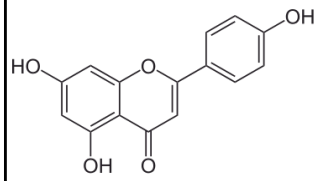


1. tumor microenvironment (stroma) influences tumor biology, treatment, and prognosis. Intra-tumor and inter-tumor microenvironment heterogenous and dynamic
2. Calon, A. et al. Stromal gene expression defines poor-prognosis subtypes in colorectal cancer; Nat Gen, 47(4) ; Apr 2015

Aneustat™ First-In-Class Multivalent Molecularly Directed Therapy (MMDT) for Cancer

- Ubiquitous use potential (tumor types, stages of disease)
- Oral drug regulated by FDA Botanical Drug Guidance for Prescription Drugs
- *Composition of matter patent: US, Canada, EU, Japan, China, Singapore*
  - *Ganoderma lucidum, Salvia miltiorrhiza, Scutellaria barbata*
- Formulated based on systems biology considerations: cell, stroma, host response
- Excellent pre-clinical safety & efficacy *in vivo*:
  - Efficacy without toxicity—therapeutic doses 10-19% of MTD (single oral)
  - Prostate tumor growth inhibition comparable to chemo but without side effects
  - Tumor shrinkage in prostate cancer (with PSA reduction) when combined with sub-therapeutic dose of docetaxel
- Phase I clinical trial data in patients with advanced treatment-refractory cancer
  - **Absence of toxicity**—no MTD or DLT observed in patients; no AE's "definitely" attributed
  - **Dose-responsive activity** against cancer pathway relating to multiple cancer hallmarks
  - Maximum therapeutic exposure—8 months

Aneustat™ (OMN54) Chemical Markers

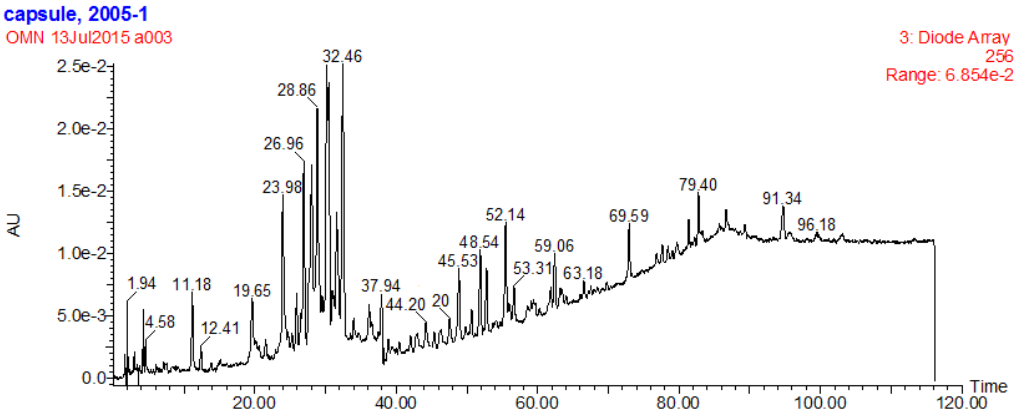
Chemical Name	Ganoderic Acid A	Tanshinone IIA	Scutellarein	Apigenin
Source	*Ganoderma lucidum*	*Salvia miltiorrhiza*	*Scutellaria barbata*	*Ganoderma lucidum* *Scutellaria barbata*
Systematic Name	(7β,15α,25R)-7,15-Dihydroxy-3,11,23-trioxolanost-8-en-26-oic acid	1,6,6-Trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-dione	5,6,7-Trihydroxy-2-(4-hydroxyphenyl)-4H-chromen-4-one	5,7-Dihydroxy-2-(4-hydroxyphenyl)-4H-chromen-4-one
Chemical Structure				
Molecular Formula	$C_{30}H_{44}O_7$	$C_{19}H_{18}O_3$	$C_{15}H_{10}O_6$	$C_{15}H_{10}O_5$
Molecular Weight	516.666199 Da	294.344391 Da	286.236298 Da	270.236908 Da

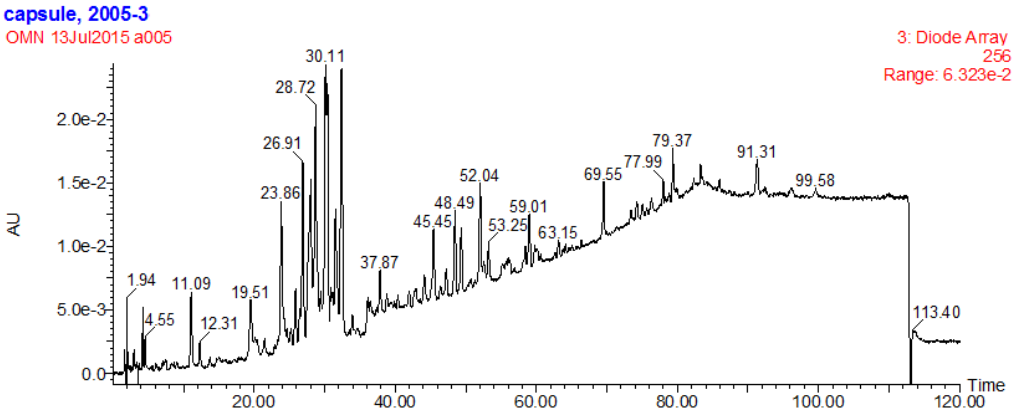
Proprietary Multicision™ Processes Ensure Aneustat™ Biochemical Equivalence

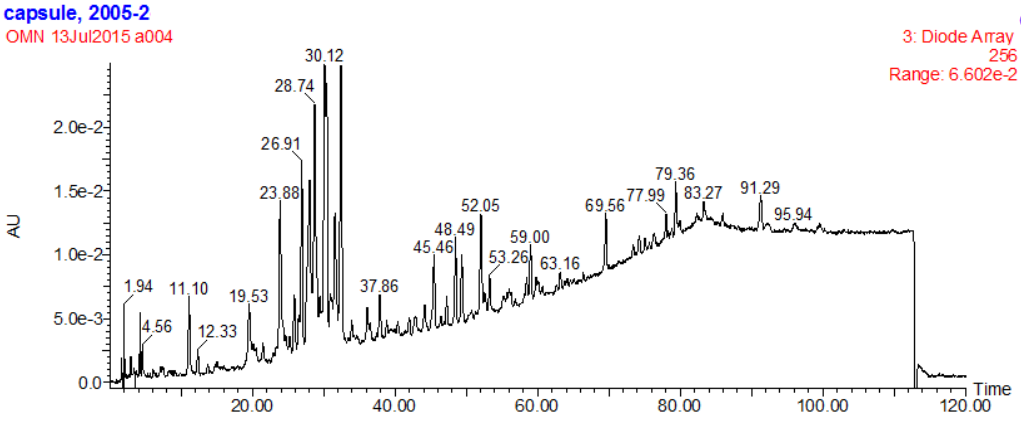
- Intra batch uniformity
- Batch to batch consistency
- Long-term stability

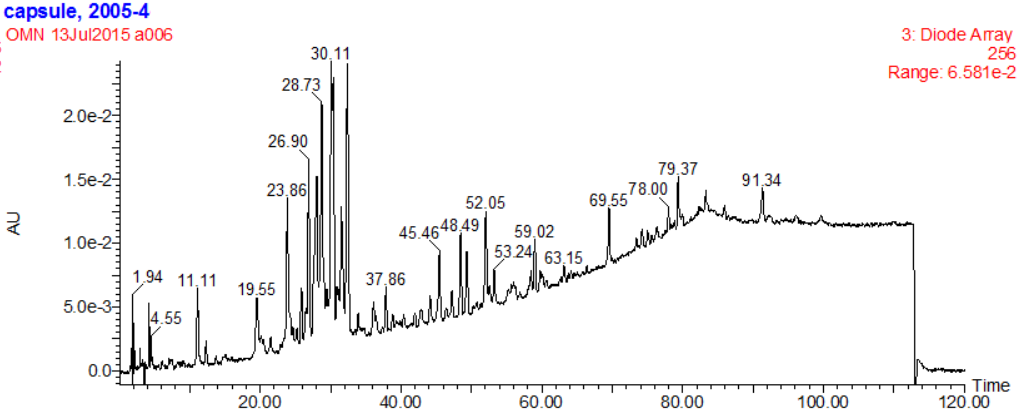
Intra Batch Drug Uniformity Test
Aneustat™ Softgel Capsules 2005

HPLC/UV (256 nm) chemical profiles of four random samples of Aneustat Softgel Capsules (2005). λmax 256 nm was used for detection of **Ganoderic Acid A** at a Retention Time of ~32 min.









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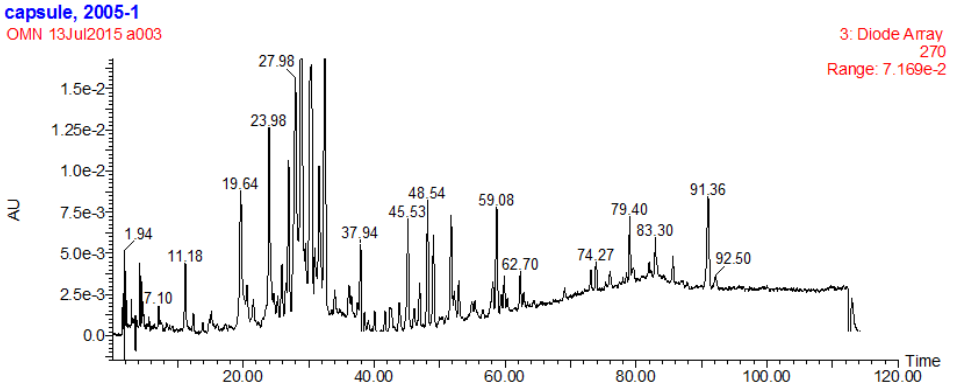

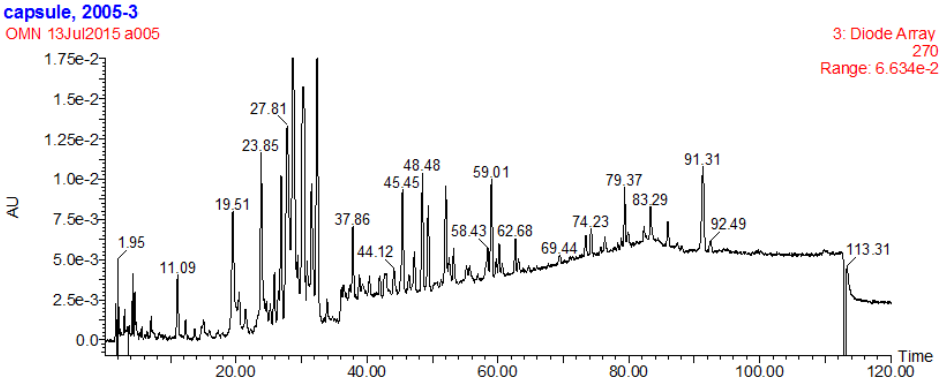

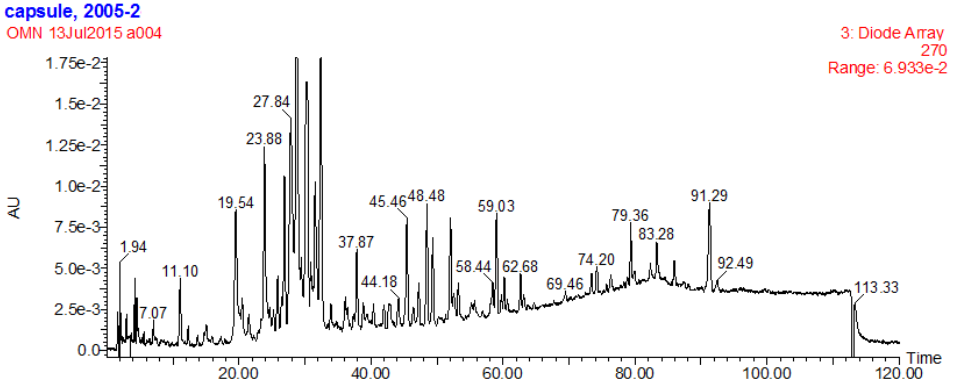

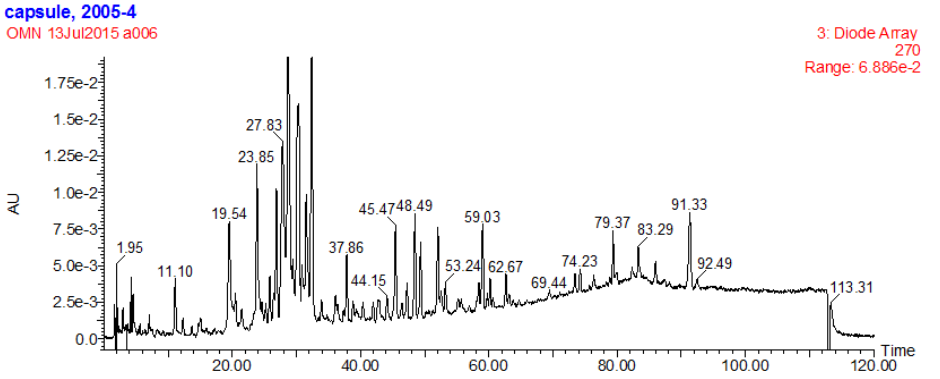

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Aneustat™ Softgel Capsules 2005

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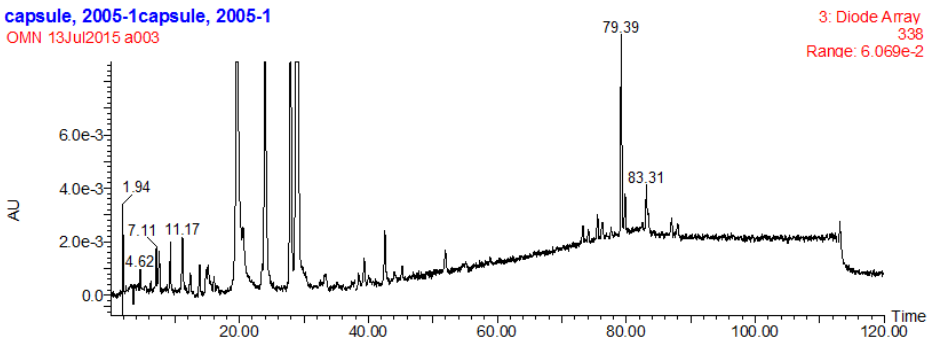

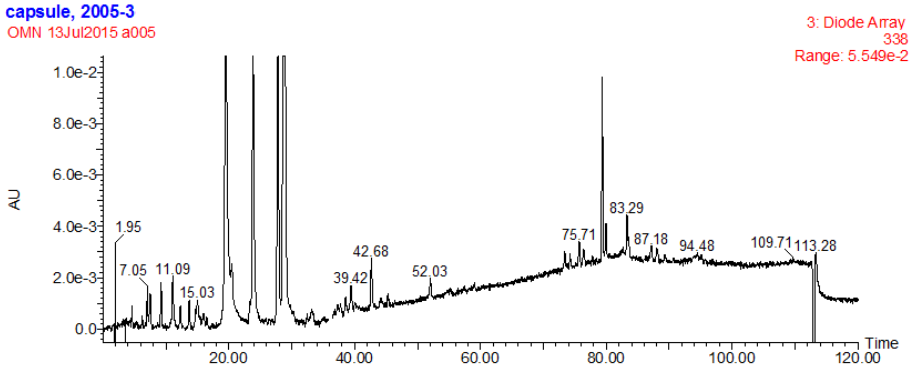

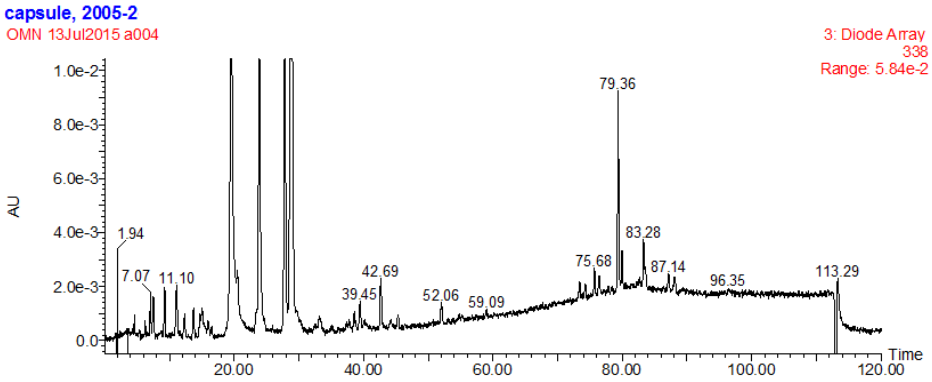

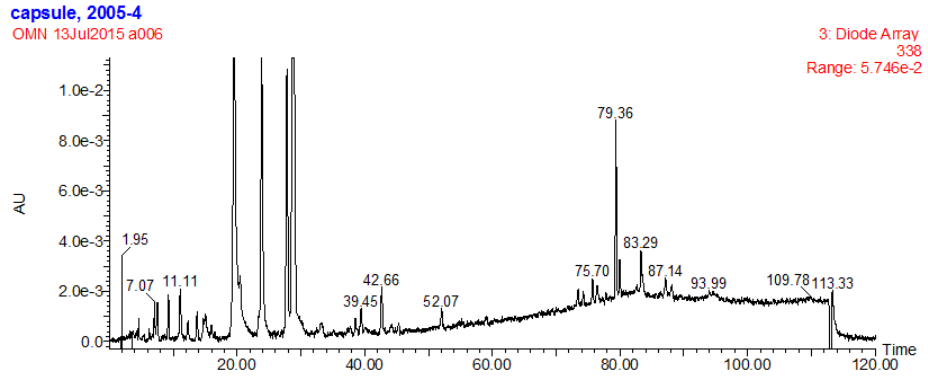

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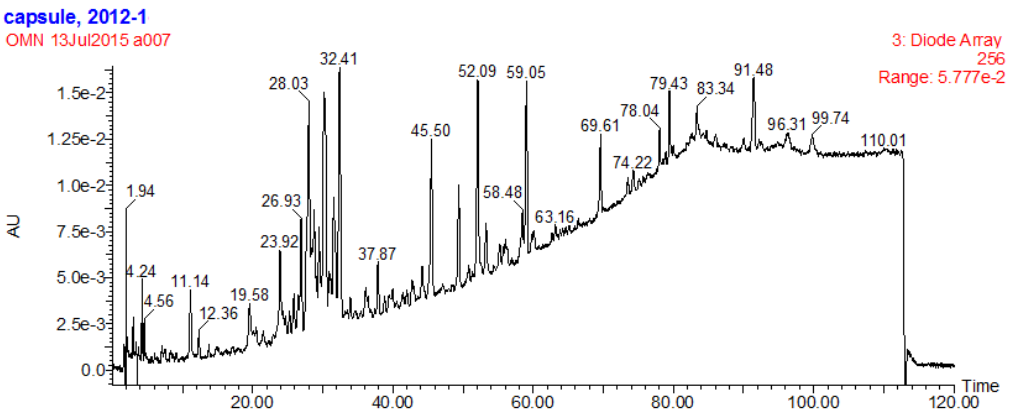

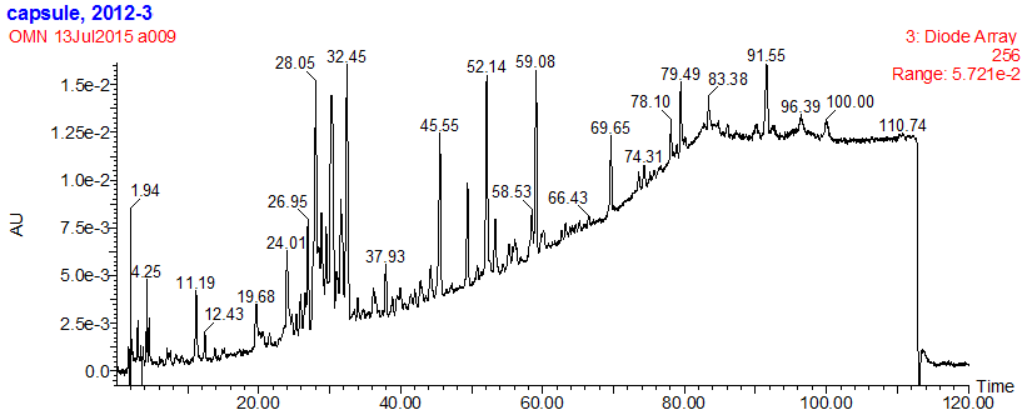

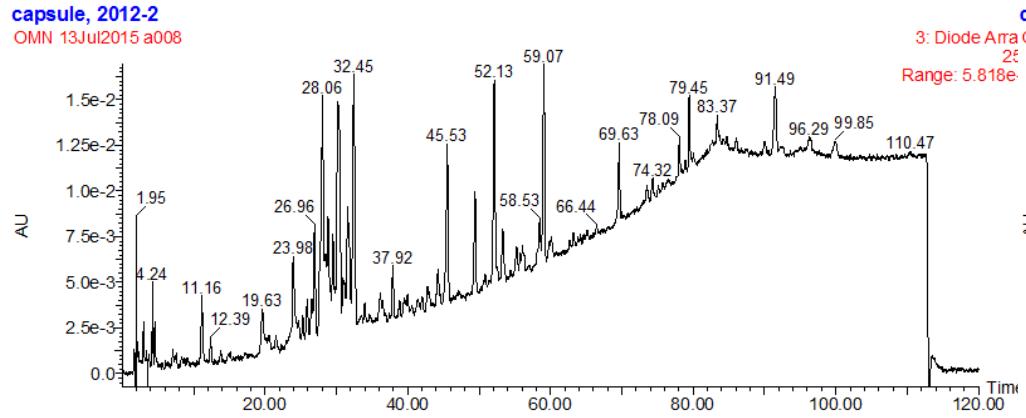

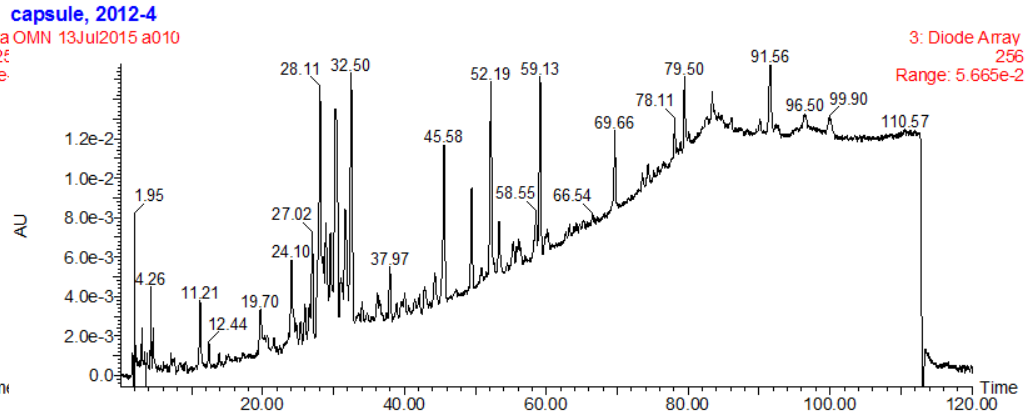

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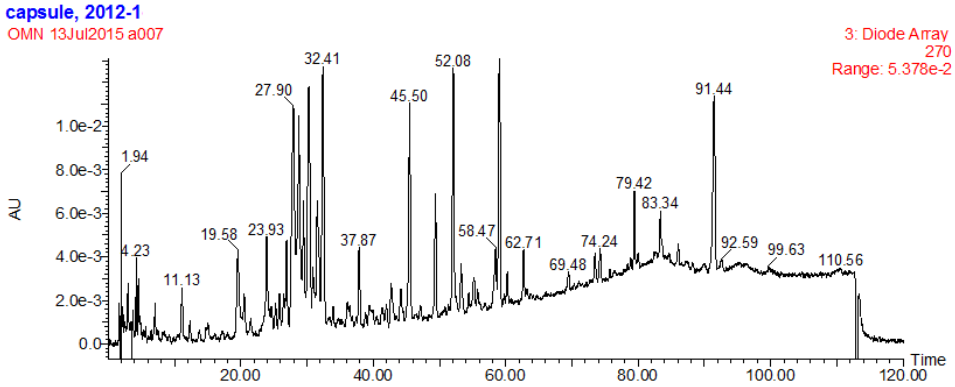

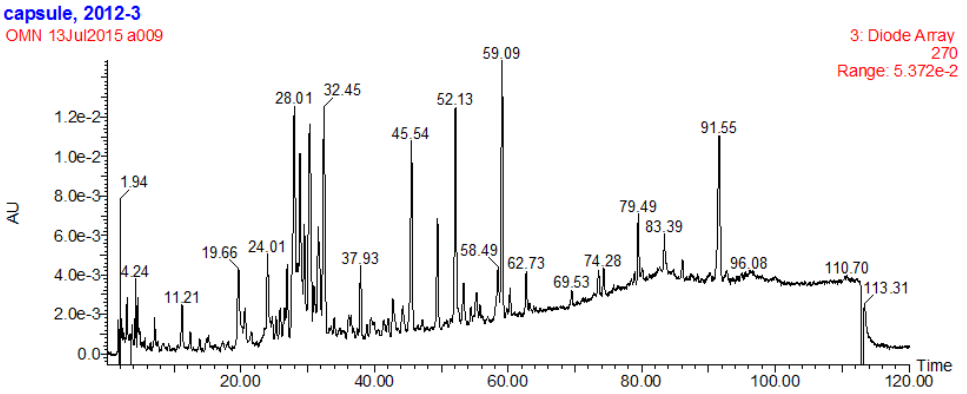

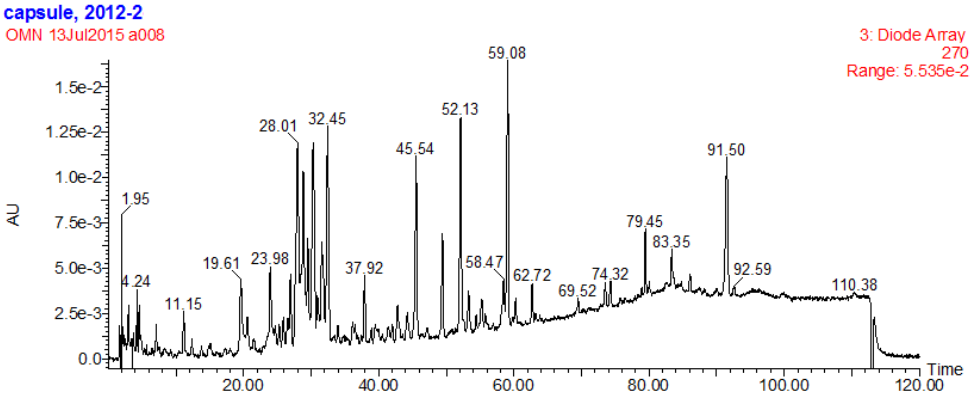

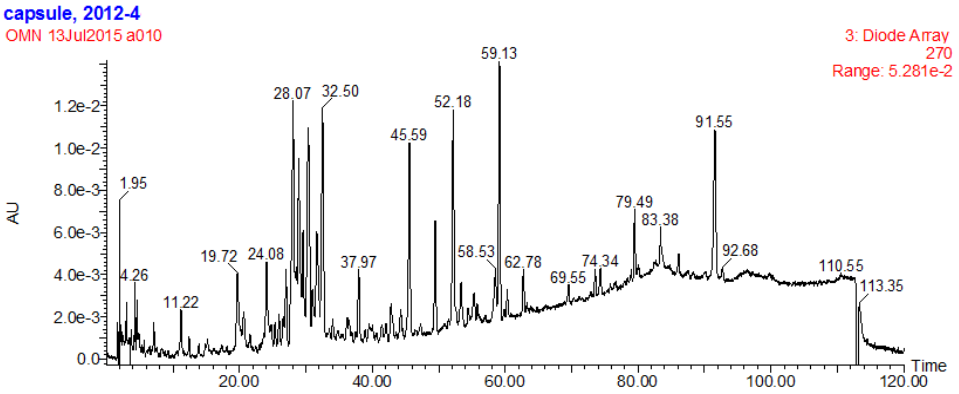

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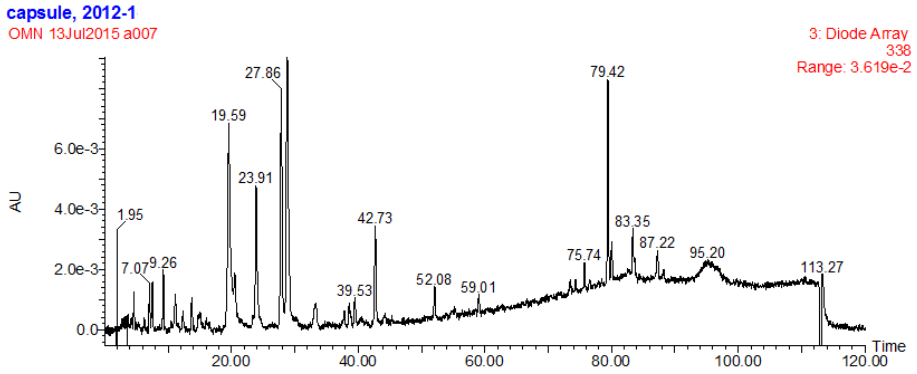

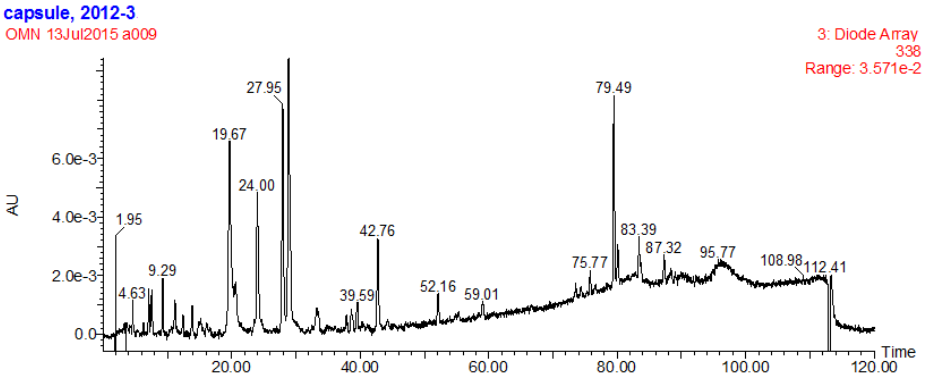

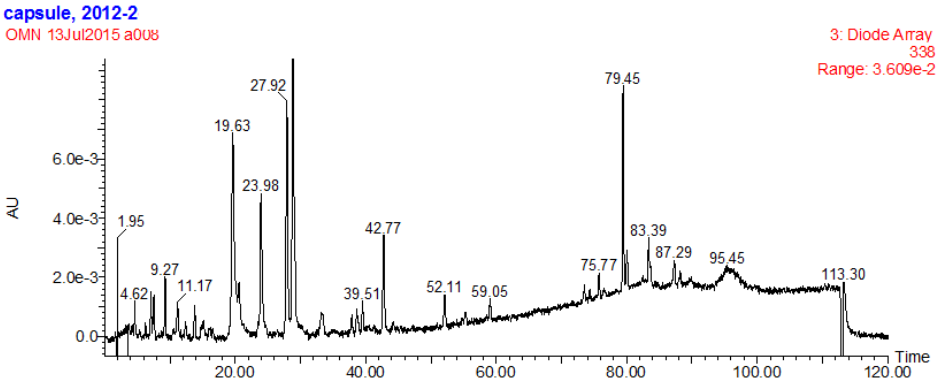

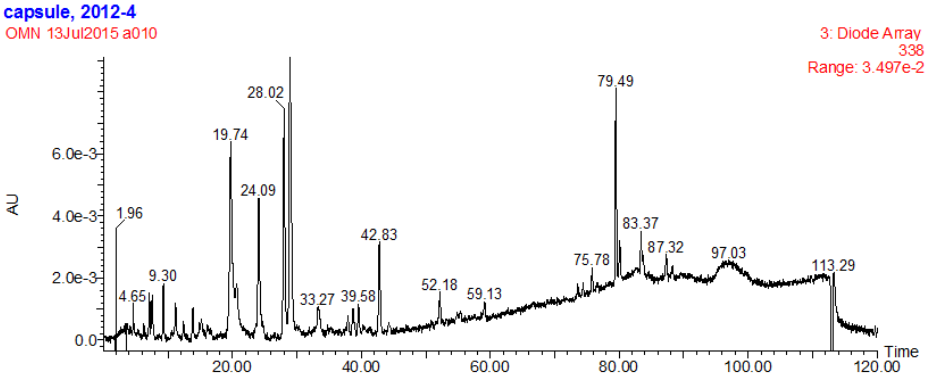

Batch to Batch Consistency and Stability Test
Aneustat™ Softgel Capsules 2005 & 2012

HPLC/UV (256 nm) chemical profiles of Aneustat Softgel Capsules (2005 & 2012 Comparison).
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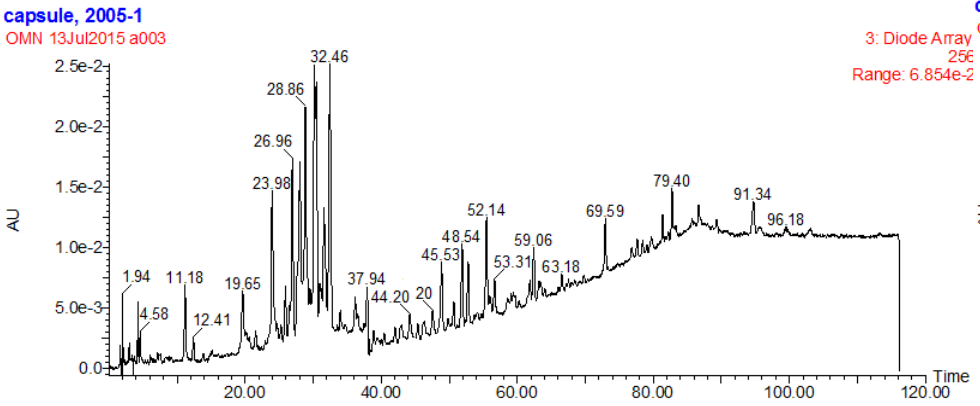
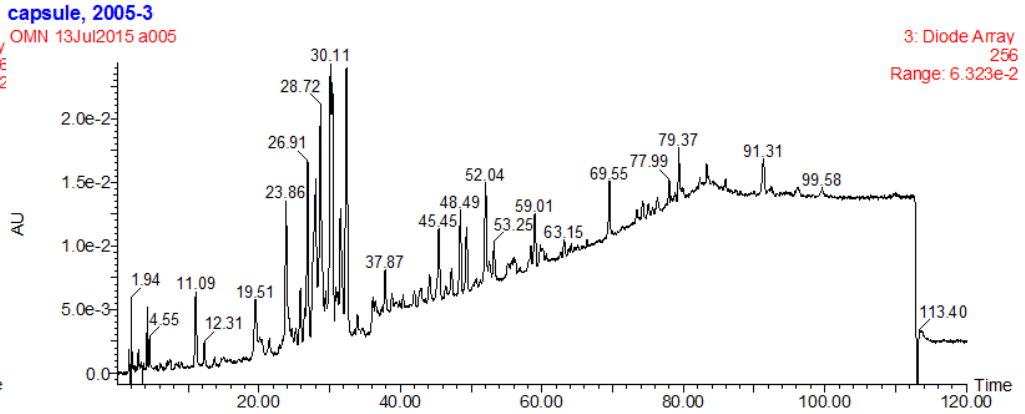
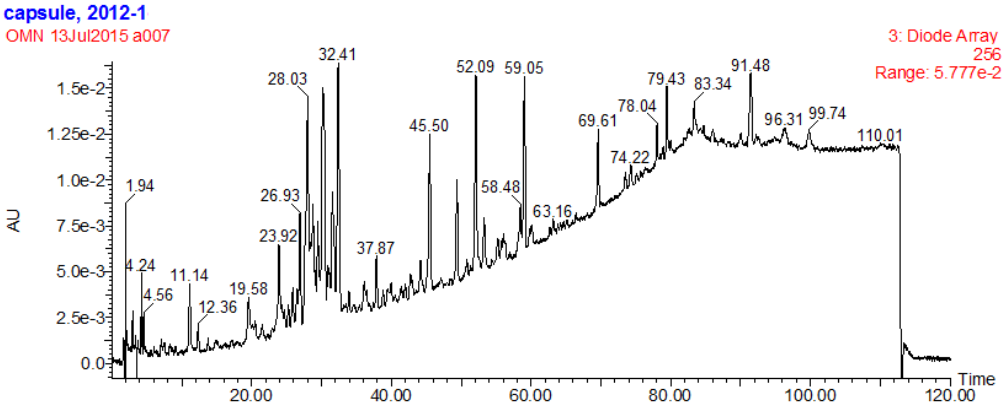
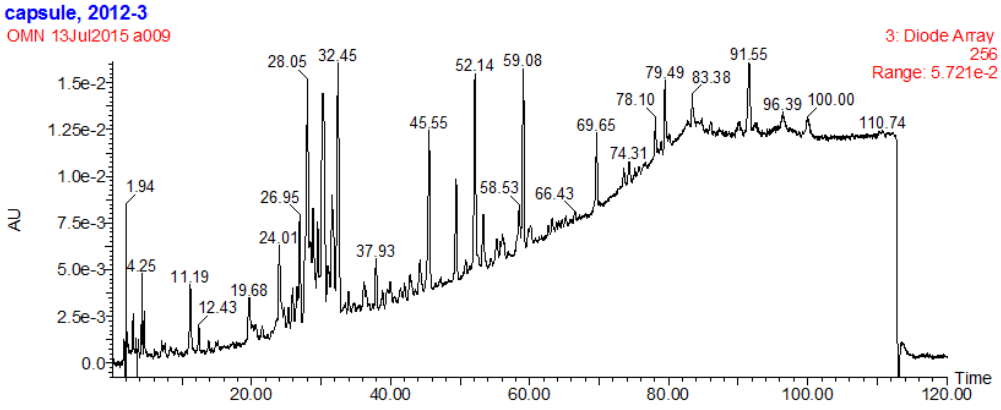
2005





2012

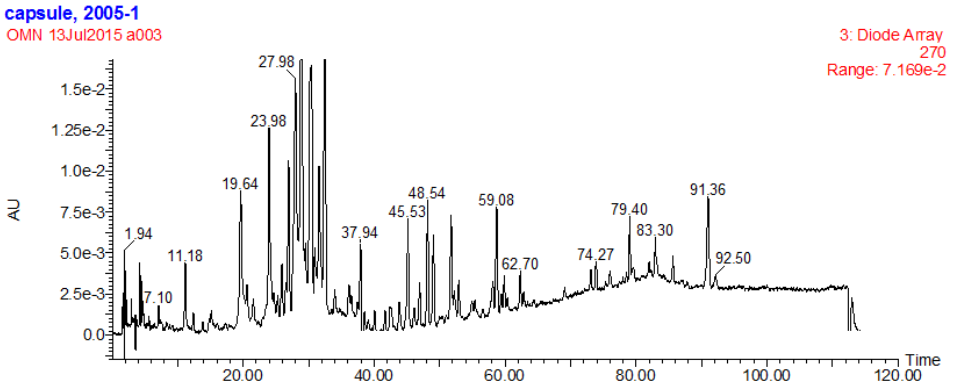


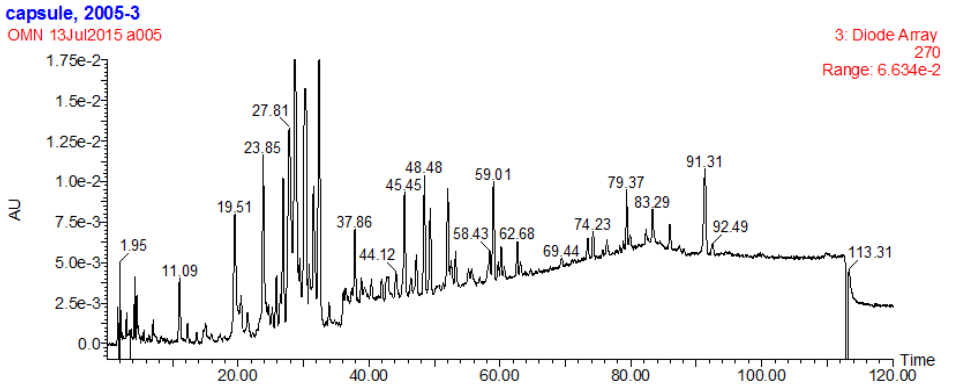


Batch to Batch Consistency and Stability Test Aneustat™ Softgel Capsules 2005 & 2012

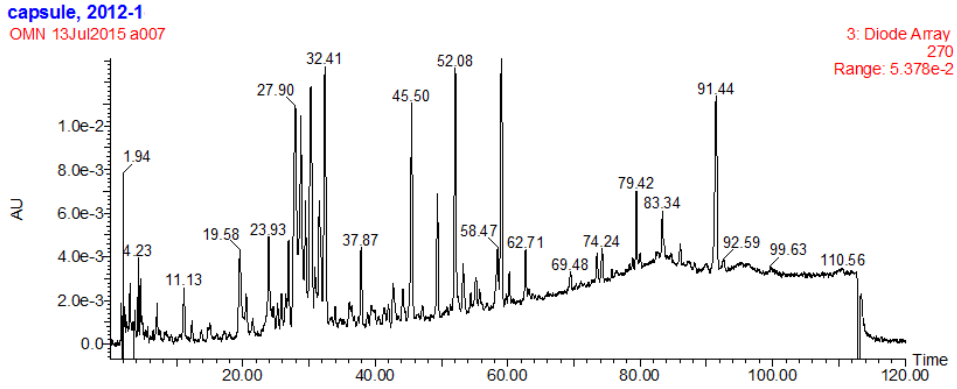
HPLC/UV (256 nm) chemical profiles of four random samples of Aneustat Softgel Capsules (2005). λmax 270 nm was used for detection of **Tanshinone II A** at a Retention Time of ~59 min.

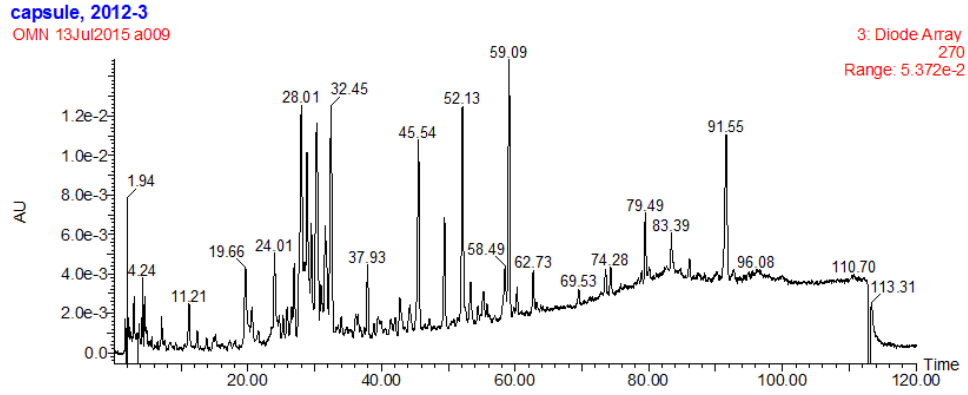
2005





2012

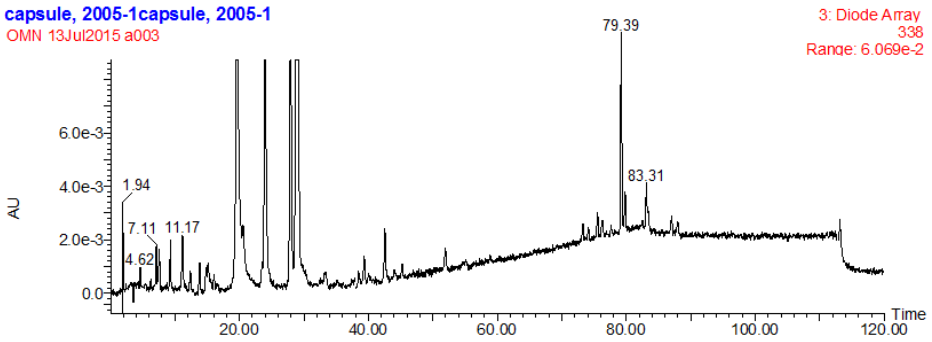


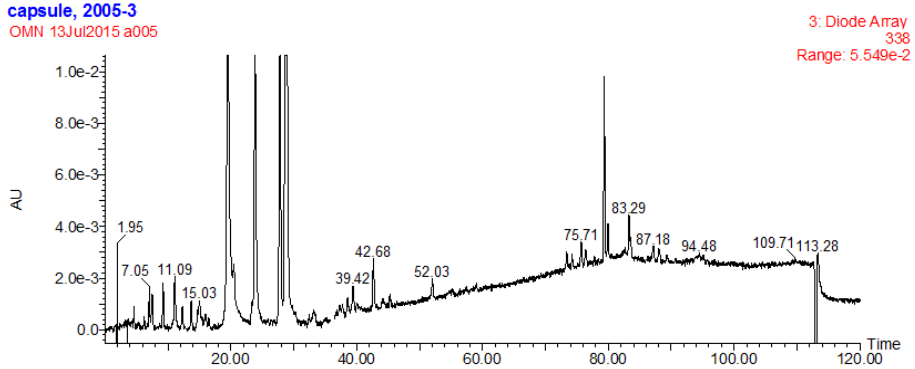


Batch to Batch Consistency and Stability Test Aneustat™ Softgel Capsules 2005 & 2012

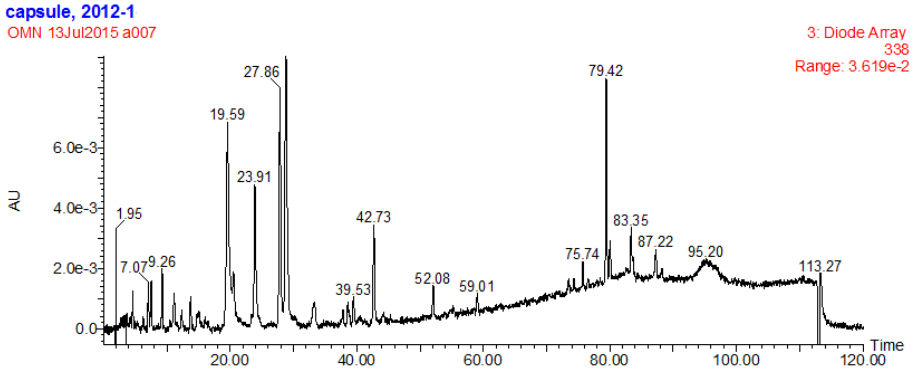
HPLC/UV (256 nm) chemical profiles of four random samples of Aneustat Softgel Capsules (2005). λmax 338 nm was used for detection of **Apigenin** at a Retention time of ~19 min and **Scutellarein** at a Retention Time of ~29 min.

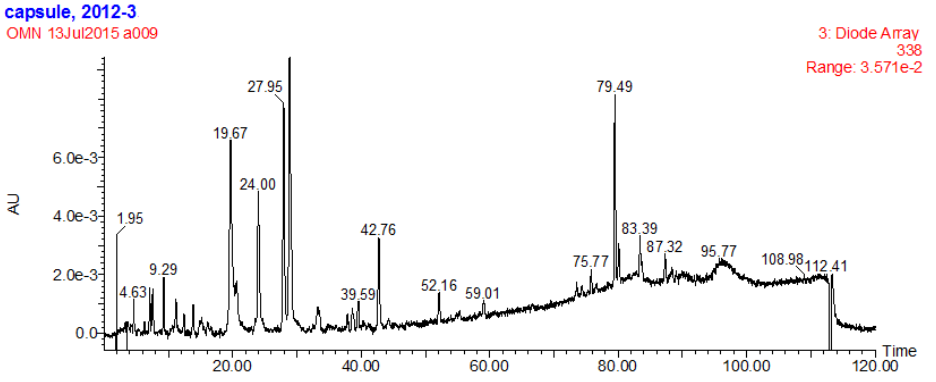
2005





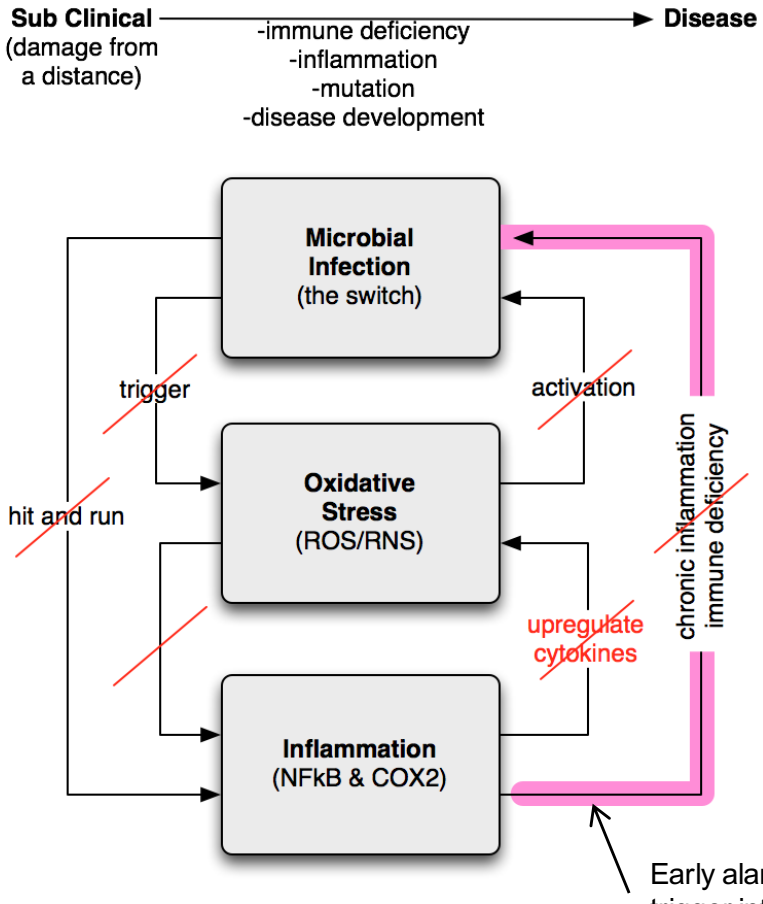
2012



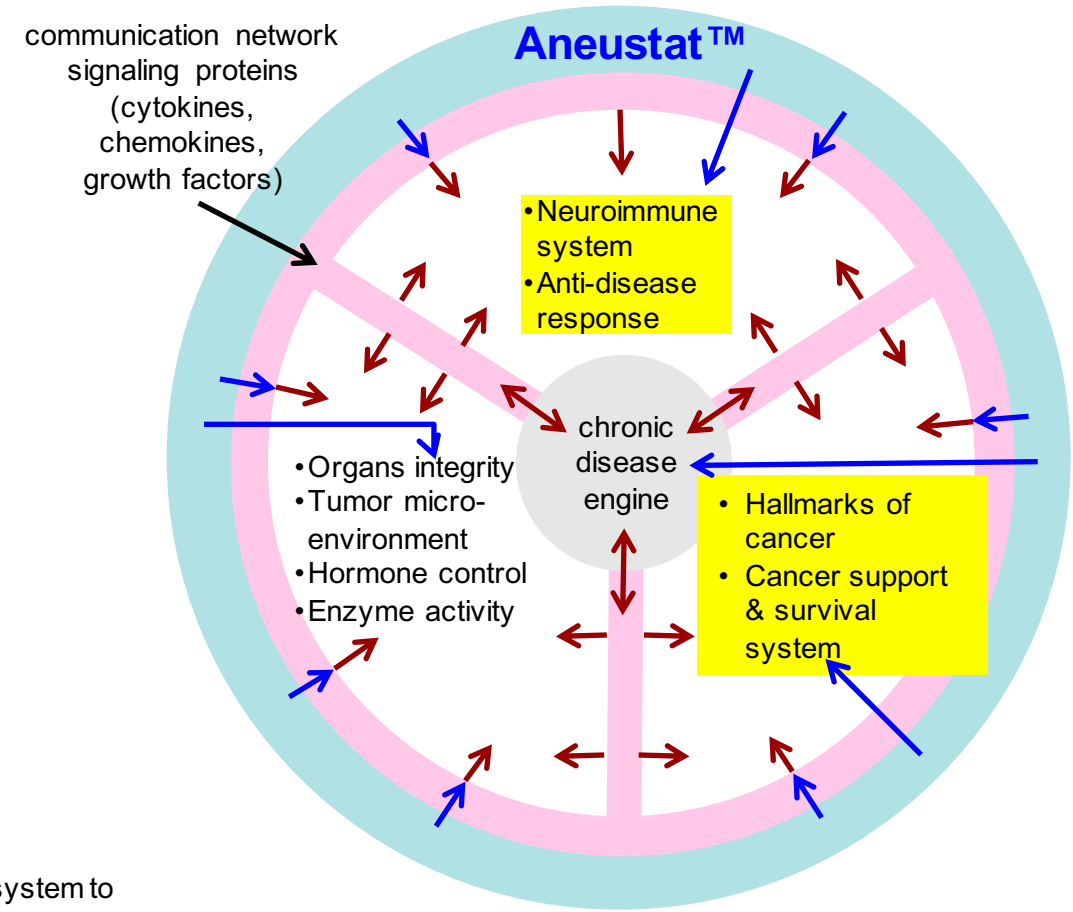


Aneustat™ has Multivalent Therapeutic Mechanisms That are Ideal for Prevention and Treatment of Cancer and Co-Existing Chronic Diseases

Aneustat™ Intercepts Cancer By Inhibiting The Chronic Disease Engine (the interplay of microbial infection, oxidative stress, and inflammation)



Aneustat™ Directly and Indirectly Modulates Key Biology Systems And Their Communication to Intercept, Treat and Prevent Cancer Proliferation



Aneustat™ is the Master Regulator of Neuroimmune Signaling—Cytokines, Chemokines and Growth Factors

- Under normal conditions, Aneustat™ neither blocks nor inhibits signaling protein expression (which avoids an adverse impact on the immune system)—ex vivo and in human
- Aneustat™ prevents or reduces mitogen stimulated overexpression of signaling proteins involved in the inflammatory response—ex vivo
- In disease states characterized by signaling protein overexpression, Aneustat™ modulates to within normal ranges (restore homeostasis & immune equilibrium)—in human

OMN54 Maintains Homeostasis of Innate Immune Response & Regulates Signaling Protein Response Ex Vivo—Key Indication of Safety

- OMN54 ($1xIC_{50}$) did not modulate pro-inflammatory cytokines in unstimulated PBMC[1] (indicating safety)[4]
- In the presence of inflammatory stimulus (PHA mitogen[2]; 48 hrs), OMN54 ($1xIC_{50}$) suppressed inflammatory signaling (significant anti-inflammatory activity)[4]

	Maintain Homeostasis		Prevent Homeostasis Disruption	
Innate Immune Response	**No Treatment** (pg/ml)	**OMN54 Treated (48 hrs)** (pg/ml)	**No Treatment** (pg/ml)	**OMN54 Treated (48 hrs)** (pg/ml)
IL1β	14.5	ND	1,100	41
IL6	25	23	14,500	687
TNFα	9.5	8.7	277	11
IL-10	8.4	7	687	6.2

IL1β: interleukin 1 beta
IL6: interleukin 6
TNFα: tumor necrosis factor alpha
IL-10: interleukin 10

[1]PBMC = Peripheral Blood Mononuclear Cells
[2]Phytohemagglutinin (PHA) Mitogen = An agent that induces mitosis (cell division)
[3]ND = not detectable (<7 pg)
[4]Measured via Luminex (Biosource/Invitrogen 25 plex)

Lab: Genyous Biomed Intl
Santa Barbara, CA

OMN54 Maintains Homeostasis of Adaptive Immune Response & Regulates Signaling Protein Response Ex Vivo—Key Indication of Safety

- OMN54 ($1xIC_{50}$) did not modulate pro-inflammatory proteins in unstimulated PBMC[1] (indicating safety)[4]
- In the presence of inflammatory stimulus (PHA mitogen[2]; 48 hrs), OMN54 ($1xIC_{50}$) suppressed inflammatory signaling (significant anti-inflammatory activity)[4]

	Maintain Homeostasis		Prevent Homeostasis Disruption	
Adaptive Immune Response	**No Treatment** (pg/ml)	**OMN54 Treated (48 hrs)** (pg/ml)	**No Treatment** (pg/ml)	**OMN54 Treated (48 hrs)** (pg/ml)
IL-12	13.7	8.2	257	9.6
IFNɣ	12	13	2,100	11
GM-CSF	5.7	6.6	189	10.4
IL-17	25	22	138	9.4
IL6	25	23	14,500	687
TGFβ	1,800	2,200	6,200	3,000
IL2ra (CD25)	25	25	707	63

IL-12: interleukin 12
IFNɣ: interferon gamma
GM-CSF: granulocyte-macrophage colony-stimulating factor
IL-17: interleukin 17
IL6: interleukin 6
TGFβ: transforming growth factor beta
IL2ra (CD25): interleukin 2 receptor alpha

[1]PBMC = Peripheral Blood Mononuclear Cells
[2]Phytohemagglutinin (PHA) Mitogen = An agent that induces mitosis (cell division)
[3]ND = not detectable (<7 pg)
[4]Measured via Luminex (Biosource/Invitrogen 25 plex)

Lab: Genyous Biomed Intl
Santa Barbara, CA

OMN54 Maintains Homeostasis of Growth Factors & Regulates Signaling Protein Response Ex Vivo—Key Indication of Safety

- OMN54 ($1xIC_{50}$) did not modulate pro-inflammatory proteins in unstimulated PBMC[1] (indicating safety)[4]
- In the presence of inflammatory stimulus (PHA mitogen[2]; 48 hrs), OMN54 ($1xIC_{50}$) suppressed inflammatory signaling (significant anti-inflammatory activity)[4]

	Maintain Homeostasis		Prevent Homeostasis Disruption	
Growth Factors/ Angiogenesis	**No Treatment** (pg/ml)	**OMN54 Treated (48hrs)** (pg/ml)	**No Treatment** (pg/ml)	**OMN54 Treated (48hrs)** (pg/ml)
VEGF	37	43	394	60
FGFβ	26	59	9.9	ND
EGF	<1	<1	21	<1

VEGF: vascular endothelial growth factor
FGFβ: fibroblast growth factor beta
EGF: epidermal growth factor

[1]PBMC = Peripheral Blood Mononuclear Cells
[2]Phytohemagglutinin (PHA) Mitogen = An agent that induces mitosis (cell division)
[3]ND = not detectable (<7 pg)
[4]Measured via Luminex (Biosource/Invitrogen 25 plex)

Lab: Genyous Biomed Intl
Santa Barbara, CA

Aneustat™ is a First-In-Class Multivalent Neuroimmune System Therapy for Cancer

What is the neuroimmune system

- **The neuroimmune system is the combined systemic interactions between neural and immune systems which regulate innate and adaptive responses against disease.**
- **It involves the immune system (APC, T, NK cells, etc.) and related components such as cytokines, neural-endocrine interactions (HPA), endorphins*, and hormonal signaling proteins (steroids); the lymphatic system connects these potent control processes.**
- **These natural responses can be augmented or modified by exogenous agents (therapy).**

Aneustat™ is a master regulator of the neuroimmune system

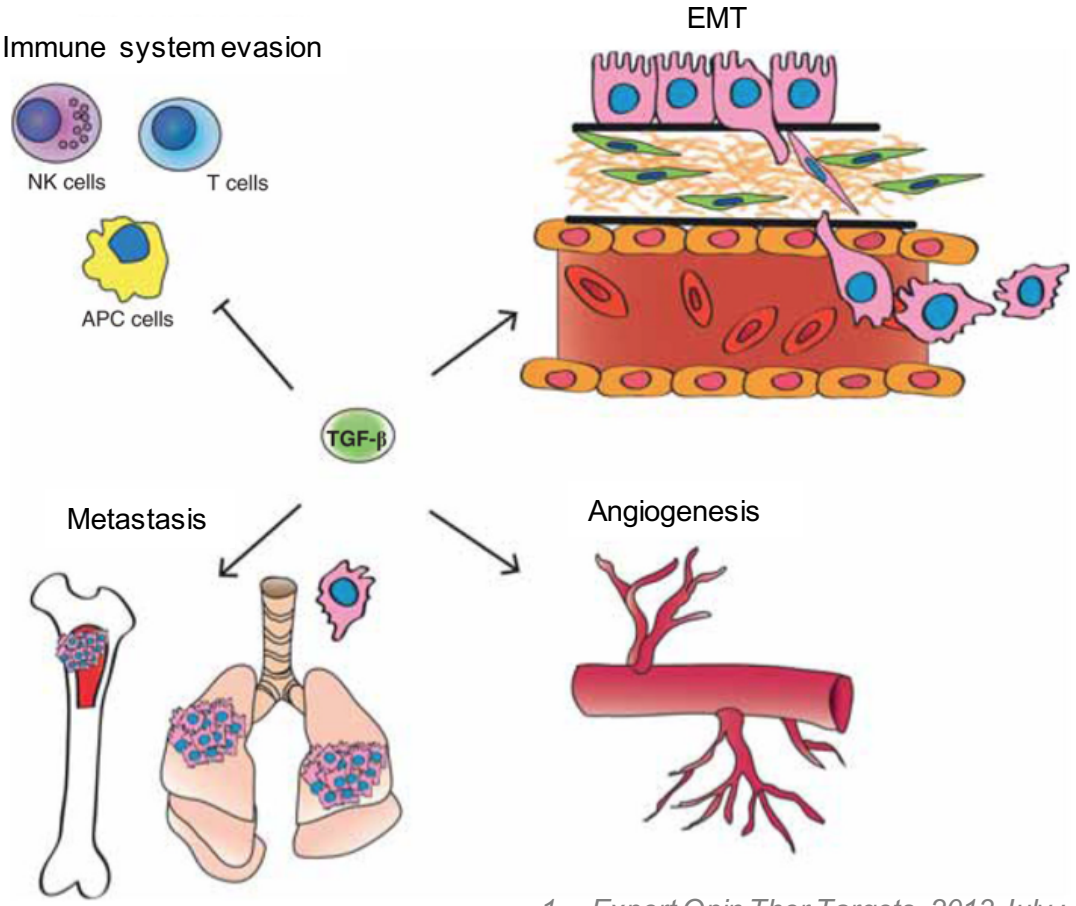
**Genetics and the placebo effect: the placebome. Hall, K et al. Trends in Molecular Medicine, 21:4, Apr 2015*

Aneustat™ Multivalent Neuroimmune System Regulator for Treating Cancer Patients

- **Aneustat™ has both direct and indirect effects on the immune system**
  - Direct effects observed include:
    - —In vitro: regulating ROS, HIF1α, NFκB, and Cyclin B
    - —Ex vivo: regulating abnormal levels of neuroimmune signaling proteins to homeostatic levels—including cytokines, chemokines, hormones, and growth factors
  - Indirect effects observed include:
    - —Ex vivo: Aneustat™ monotherapy inhibits proliferation and induces apoptosis in prostate epithelial cells
    - —In vivo: as combination therapy, regulates cellular energetics and tumor cell proliferation—aerobic
    - —In vivo: reduce production of lactic acid. Secreted lactic acid causes the tumor microenvironment to become more acidic and thus hostile to intratumoral immune response—anaerobic
  - Clinical trial in patients with advanced treatment-refractory cancer, Aneustat™ regulated TGF-β, EGF and RANTES in a dose-responsive manner to restore immune equilibrium

Transforming Growth Factor beta (TGF-β) Signaling in Tumor Promotion

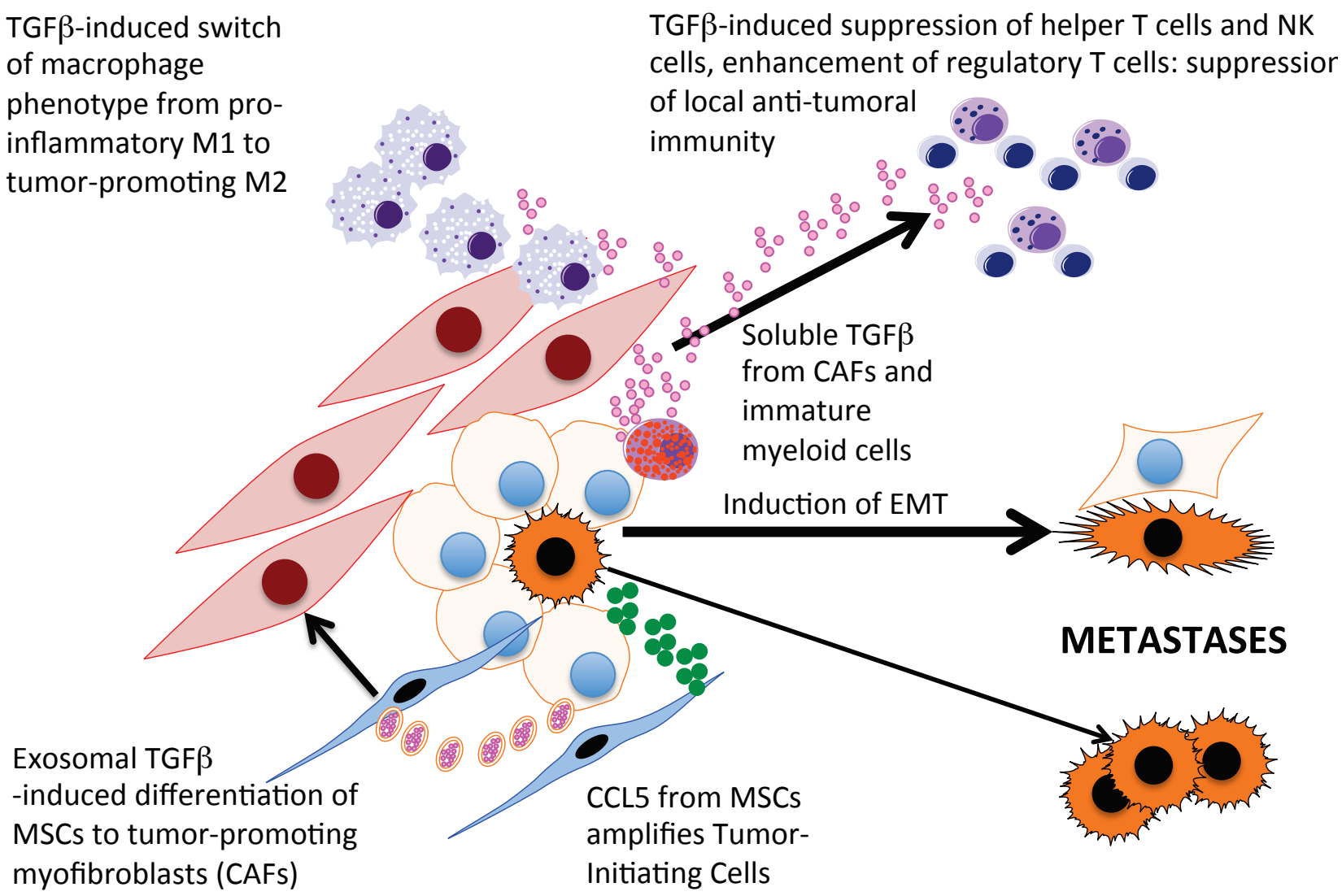
- **Abnormally high TGF-β achieves its tumor promoting effect by several mechanisms: evasion of the immune system, promotion of cancer cell proliferation, angiogenesis and EMT effect on the metastatic process by modulation of both the tumor and tumor microenvironment.[1]**



APC: Antigen presenting cells
NK: Natural killer
EMT: Epithelial-to-mesenchymal transition

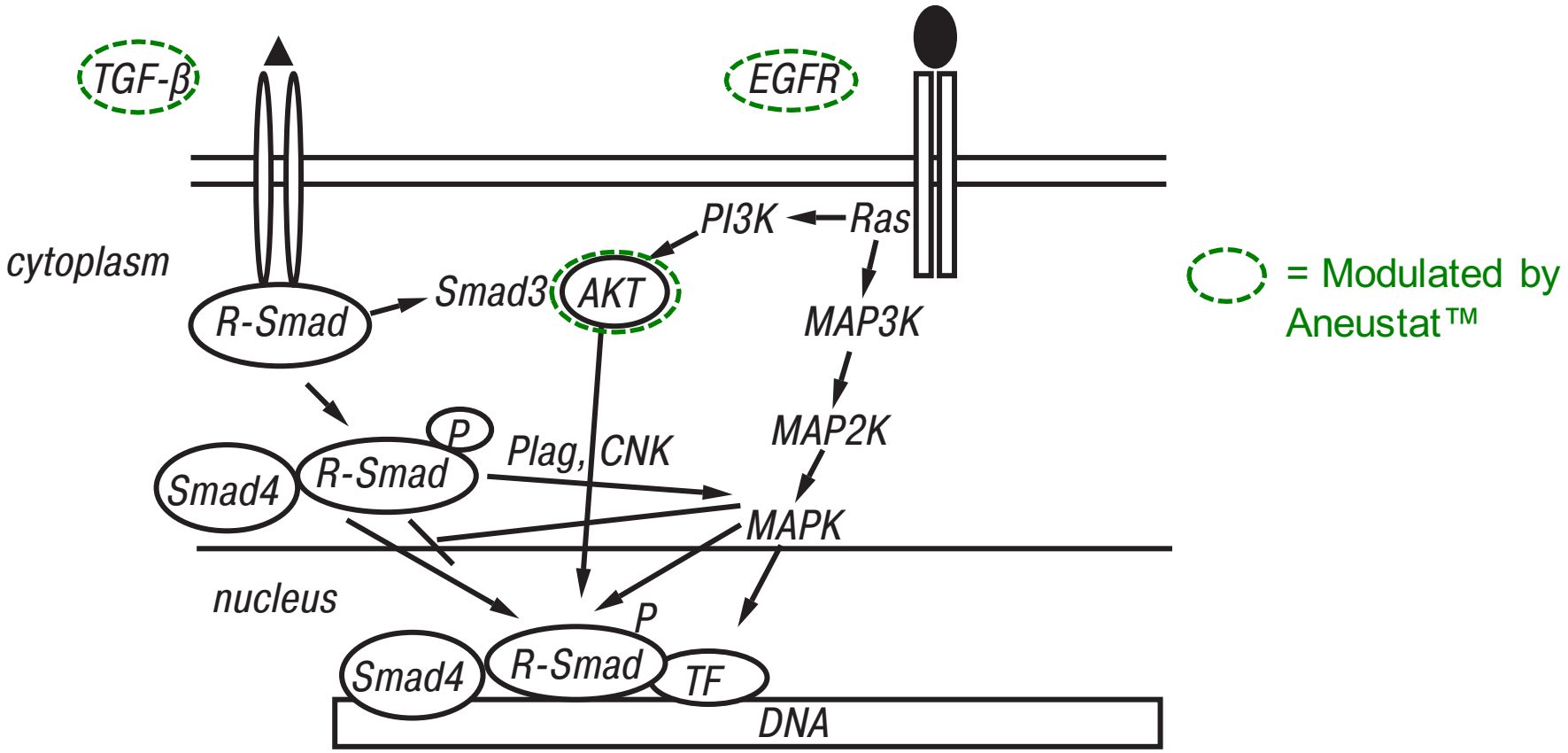
1. *Expert Opin Ther Targets. 2013 July ; 17(7): 743–760*

Cross-talk Between TGF-β and Rantes (CCL5) Signaling Pathway Promotes Tumor Initiating Cells



Maitland, NJ (2015) Carcinoma-derived exosomes act as microenvironment modifiers in prostate cancer. Oncotarget (in press)

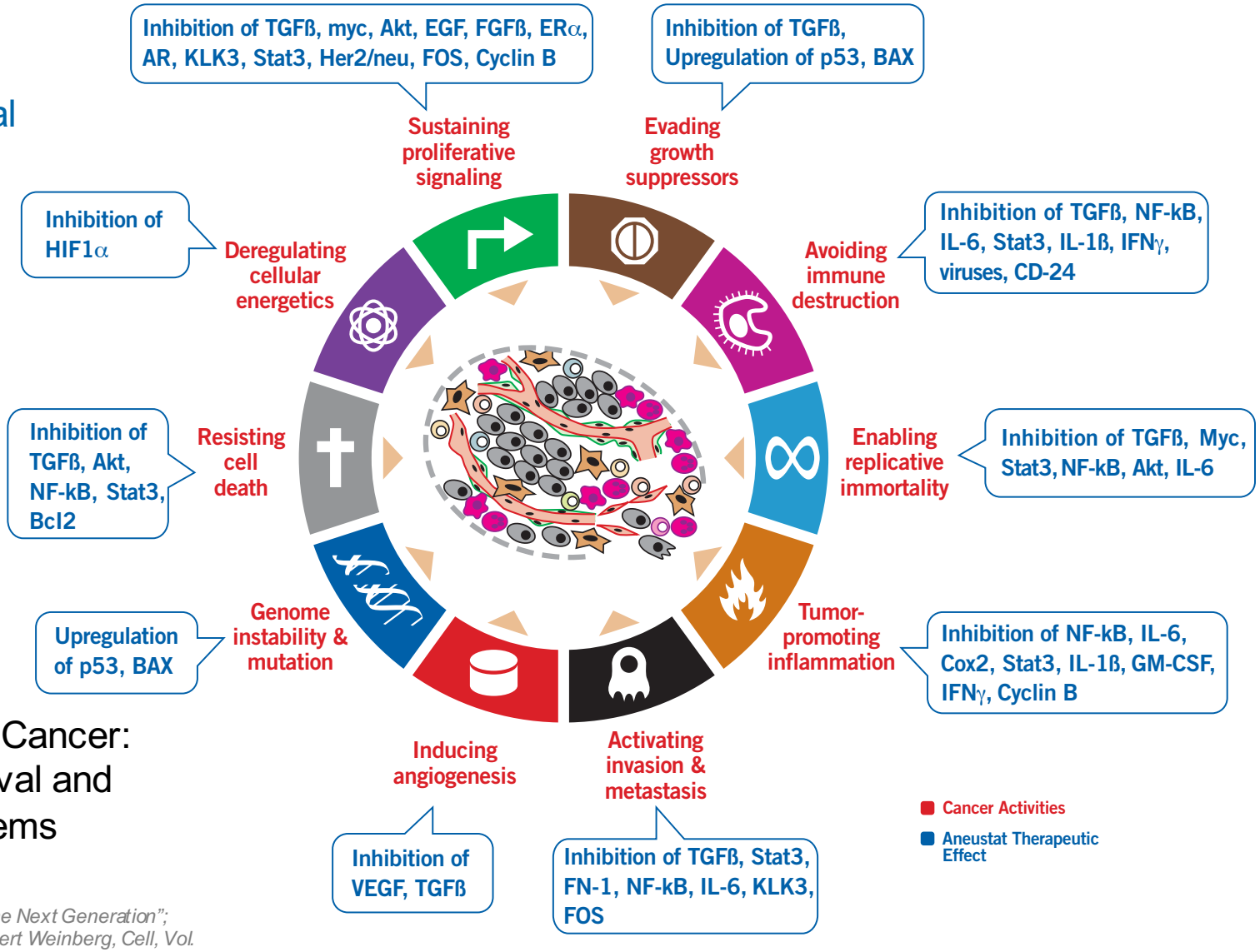
Cross-talk Between TGF-β and EGF Signaling Pathways Increase Tumorigenesis



Exp Oncol 2011 33, 3, 170–173

Aneustat™ is a Master Controller of the Hallmarks of Cancer in Cancer Cell and Tumor Microenvironment

Based on experimental data



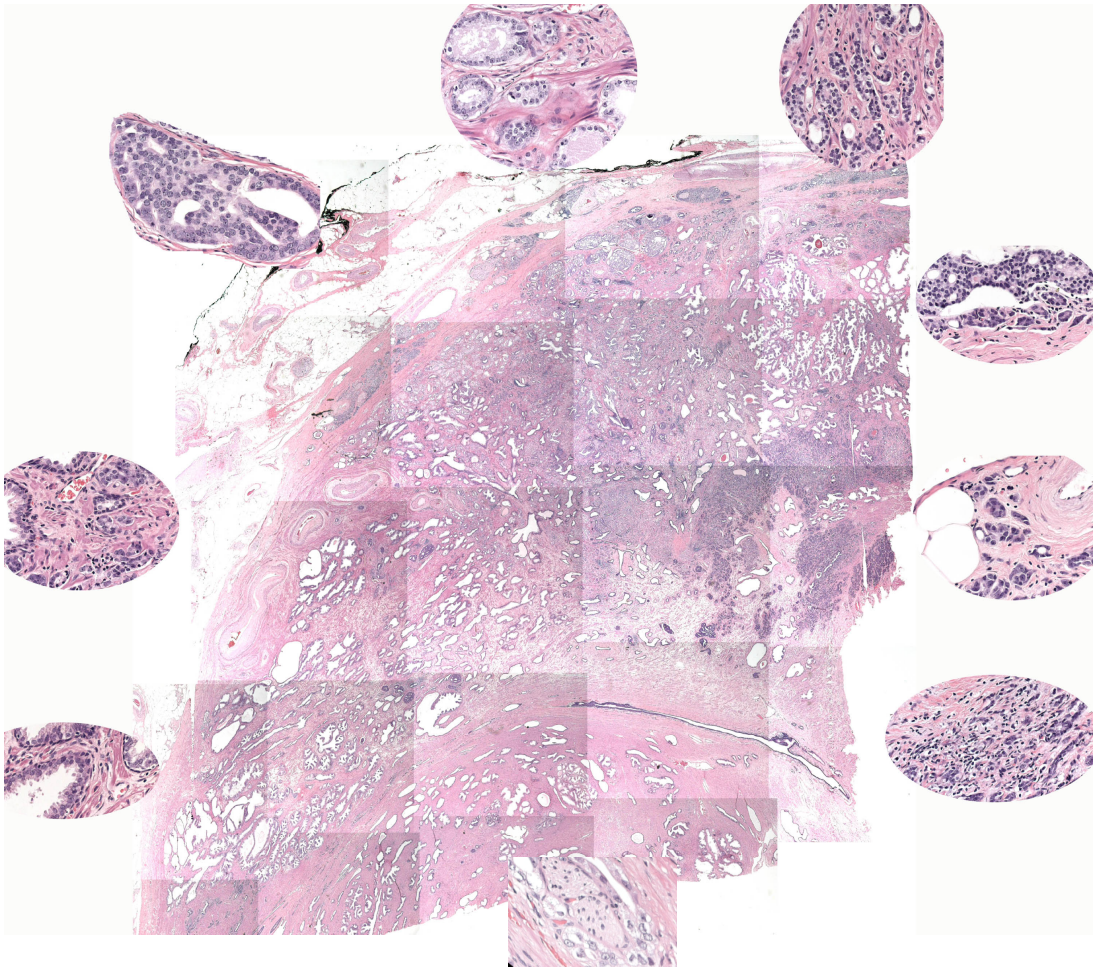
Hallmarks of Cancer: Cancer survival and support systems

Adapted from:
"Hallmarks of Cancer: The Next Generation";
Douglas Hanahan & Robert Weinberg, Cell, Vol. 144, 648–674, March, 2011

Hallmarks of Cancer Literature

Hallmarks of Cancer			
Signaling	**Molecular Markers**	**PMID**	**Reference**
Sustaining proliferative signaling	TGF β	8983080	TGF beta regulation of cell proliferation.Princess Takamatsu Symp. 1994;24:250-63.
	Myc	23071356	c-Myc and cancer metabolism.Clin Cancer Res. 2012 Oct 15;18(20):5546-53.
	AKT	10363971	Regulation of Akt/PKB activity, cellular growth, and apoptosis in prostate carcinoma cells by MMAC/PTEN.Cancer Res. 1999 Jun 1;59(11):2551-6.
	EGF	25711523	Fhit Nuclear Import Following EGF Stimulation Sustains Proliferation of Breast Cancer Cells.J Cell Physiol. 2015 Nov;230(11):2661-70.
	FGF β	20094046	Fibroblast growth factor signalling: from development to cancer.Nat Rev Cancer. 2010 Feb;10(2):116-29.
	ER α	25436982	Estrogen receptor alpha drives proliferation in PTEN-deficient prostate carcinoma by stimulating survival signaling, MYC expression and altering glucose sensitivity. Oncotarget. 2015 Jan 20;6(2):604-16.
	AR	11861374	Disruption of androgen receptor function inhibits proliferation of androgen-refractory prostate cancer cells.Cancer Res. 2002 Feb 15;62(4):1008-13.
	KLK3	26343558	The kallikrein-related peptidase family: Dysregulation and functions during cancer progression.Biochimie. 2015 Sep 4. pii: S0300-9084(15)00277-1.
	STAT3	12111703	Stat3 enhances the growth of LNCaP human prostate cancer cells in intact and castrated male nude mice.Prostate. 2002 Jul 1;52(2):123-9.
	Her2/neu	26484103	The HER2 amplicon includes several genes required for the growth and survival of HER2 positive breast cancer cells - A data description.Genom Data. 2014 Jul 22;2:249-53.
	FOS	16027729	cFos is critical for MCF-7 breast cancer cell growth.Oncogene. 2005 Sep 29;24(43):6516-24.
	Cycin B	15208674	Cyclin B1 depletion inhibits proliferation and induces apoptosis in human tumor cells.Oncogene. 2004 Jul 29;23(34):5843-52.
Evading growth suppressors	TGF β	19237272	Mechanism of TGF-beta signaling to growth arrest, apoptosis, and epithelial-mesenchymal transition.Curr Opin Cell Biol. 2009 Apr;21(2):166-76.
	p53	16094360	Evasion of the p53 tumour surveillance network by tumour-derived MYC mutants.Nature. 2005 Aug 11;436(7052):807-11.
	BAX	11861374	Deregulation of apoptotic factors Bcl-xL and Bax confers apoptotic resistance to myeloid-derived suppressor cells and contributes to their persistence in cancer.J Biol Chem. 2013 Jun 28;288(26):19103-15.
Avoiding immune destruction	TGF β	11590434	Immune-mediated eradication of tumors through the blockade of transforming growth factor-beta signaling in T cells.Nat Med. 2001 Oct;7(10):1118-22.
	NF-κB	16175180	NF-kappaB: linking inflammation and immunity to cancer development and progression.Nat Rev Immunol. 2005 Oct;5(10):749-59.
	IL-6	12220549	IL-6 in autoimmune disease and chronic inflammatory proliferative disease.Cytokine Growth Factor Rev. 2002 Aug-Oct;13(4-5):357-68.
	STAT3	16288283	Inhibiting Stat3 signaling in the hematopoietic system elicits multicomponent antitumor immunity.Nat Med. 2005 Dec;11(12):1314-21.
	IL-1β	12791316	IL-1beta, IFN-gamma and TNF-alpha increase vulnerability of pancreatic beta cells to autoimmune destruction.J Autoimmun. 2003 Jun;20(4):303-12.
	IFNγ	10936062	Immune-inflammatory mechanisms in IFNgamma-mediated anti-tumor activity.Semin Cancer Biol. 2000 Apr;10(2):113-23.
	CD-24	25752522	Variations in genes involved in immune response checkpoints and association with outcomes in patients with resected colorectal liver metastases.Pharmacogenomics J. 2015 Mar 10. doi: 10.1038/tpj.2015.14.
Enabling replicative immortality	TGF β	19237272	Mechanism of TGF-beta signaling to growth arrest, apoptosis, and epithelial-mesenchymal transition.Curr Opin Cell Biol. 2009 Apr;21(2):166-76.
	Myc	25893605	Telomerase regulates MYC-driven oncogenesis independent of its reverse transcriptase activity.J Clin Invest. 2015 May;125(5):2109-22.
	STAT3	17615260	Physiologically achievable concentrations of genistein enhance telomerase activity in prostate cancer cells via the activation of STAT3.Carcinogenesis. 2007 Nov;28(11):2282-90.
	NF-κB	20864668	Nuclear factor {kappa}B-mediated transactivation of telomerase prevents intimal smooth muscle cell from replicative senescence during vascular repair.Arterioscler Thromb Vasc Biol. 2010 Dec;30(12):2604-10.
	AKT	26178664	Expression of human telomerase reverse transcriptase mediates the senescence of mesenchymal stem cells through the PI3K/AKT signaling pathway.Int J Mol Med. 2015 Sep;36(3):857-64.
	IL-6	19802007	Cytokine expression and signaling in drug-induced cellular senescence.Oncogene. 2010 Jan 14;29(2):273-84.
Tumor promoting inflammation	NF-κB	23483479	NF-κB and STAT3 signaling pathways collaboratively link inflammation to cancer.Protein Cell. 2013 Mar;4(3):176-85.
	IL-6	16199153	The role of IL-6 and STAT3 in inflammation and cancer.Eur J Cancer. 2005 Nov;41(16):2502-12.
	Cox-2	19946329	The role of COX-2 in intestinal inflammation and colorectal cancer.Oncogene. 2010 Feb 11;29(6):781-8.
	STAT3	23483479	NF-κB and STAT3 signaling pathways collaboratively link inflammation to cancer.Protein Cell. 2013 Mar;4(3):176-85.
	IL-1β	17283139	Interleukin-1beta-driven inflammation promotes the development and invasiveness of chemical carcinogen-induced tumors.Cancer Res. 2007 Feb 1;67(3):1062-71.
	GM-CSF	12490959	Inflammation and cancer.Nature. 2002 Dec 19-26;420(6917):860-7.
Activating invasion and metastasis	TGF β	26022606	TGFβ Induces a Pro-Bone Metastasis Program in Prostate Cancer.Cancer Discov. 2015 Jul;5(7):OF23.
	STAT3	15116091	Stat3 activation regulates the expression of matrix metalloproteinase-2 and tumor invasion and metastasis.Oncogene. 2004 Apr 29;23(20):3550-60.
	NF-κB	14743471	Expression of NF-kappaB in prostate cancer lymph node metastases.Prostate. 2004 Feb 15;58(3):308-13.
	IL-6	21976712	IL-6 promotes head and neck tumor metastasis by inducing epithelial-mesenchymal transition via the JAK-STAT3-SNAIL signaling pathway.Mol Cancer Res. 2011 Dec;9(12):1658-67.
	KLK3	19819870	Functional roles of human kallikrein-related peptidases. Biol Chem. 2009 Nov 27;284(48):32989-94.
	FOS	7970719	Fos-transformation activates genes associated with invasion.Oncogene. 1994 Dec;9(12):3591-600.
Inducing angiogenesis	VEGF	16301830	VEGF as a key mediator of angiogenesis in cancer.Oncology. 2005;69 Suppl 3:4-10.
	TGF β	9721065	Transforming growth factor beta1 is associated with angiogenesis, metastasis, and poor clinical outcome in prostate cancer.Prostate. 1998 Sep 15;37(1):19-29.
Genome instability and mutation	p53	11156366	Oncogenic mutations of the p53 tumor suppressor: the demons of the guardian of the genome.Cancer Res. 2000 Dec 15;60(24):6788-93.
	BAX	9020077	Somatic frameshift mutations in the BAX gene in colon cancers of the microsatellite mutatorphenotype.Science. 1997 Feb 14;275(5302):967-9.
Resisting cell death	TGF β	8864119	TNF- and cancer therapy-induced apoptosis: potentiation by inhibition of NF-kappaB.1996 Nov 1;274(5288):784-7.
	AKT	12646949	Involvement of PI3K/Akt pathway in cell cycle progression, apoptosis, and neoplastic transformation: a target for cancer chemotherapy.Leukemia. 2003 Mar;17(3):590-603.
	NF-κB	8864119	TNF- and cancer therapy-induced apoptosis: potentiation by inhibition of NF-kappaB.Science. 1996 Nov 1;274(5288):784-7.
	STAT3	12438264	Constitutive activation of Stat3 in human prostate tumors and cell lines: direct inhibition of Stat3signaling induces apoptosis of prostate cancer cells.Cancer Res. 2002 Nov 15;62(22):6659-66.
	Bcl2	10197582	BCL-2 gene family and the regulation of programmed cell death.Cancer Res. 1999 Apr 1;59(7 Suppl):1693s-1700s.
Deregulating cellular energertics	HIF 1α	26474388	Suppression of mitochondrial respiration with auraptene inhibits the progression of renal cellcarcinoma: involvement of HIF-1α degradation.Oncotarget. 2015 Oct 12.

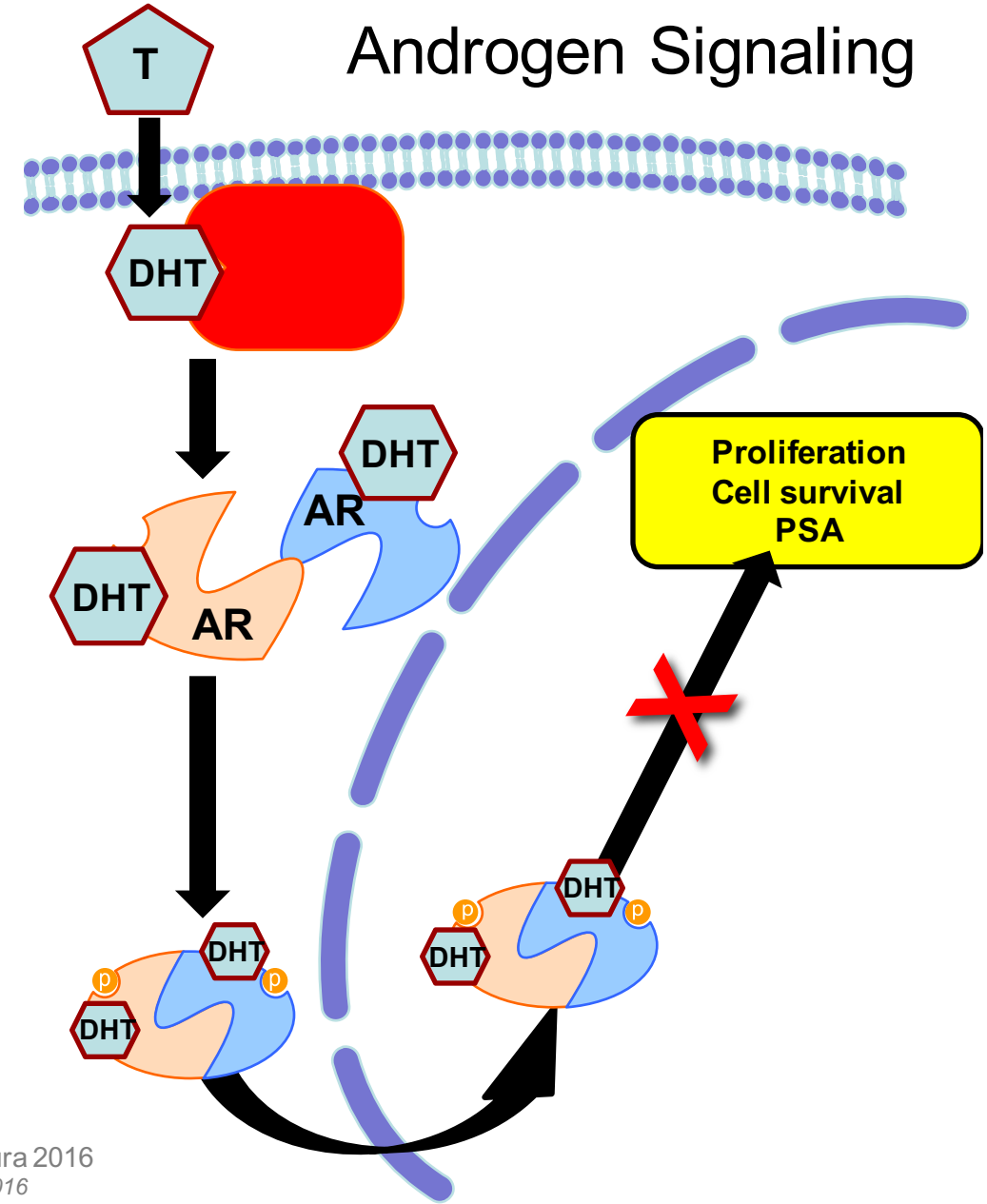
Clinical Cancer/Human Tumors are Heterogeneous



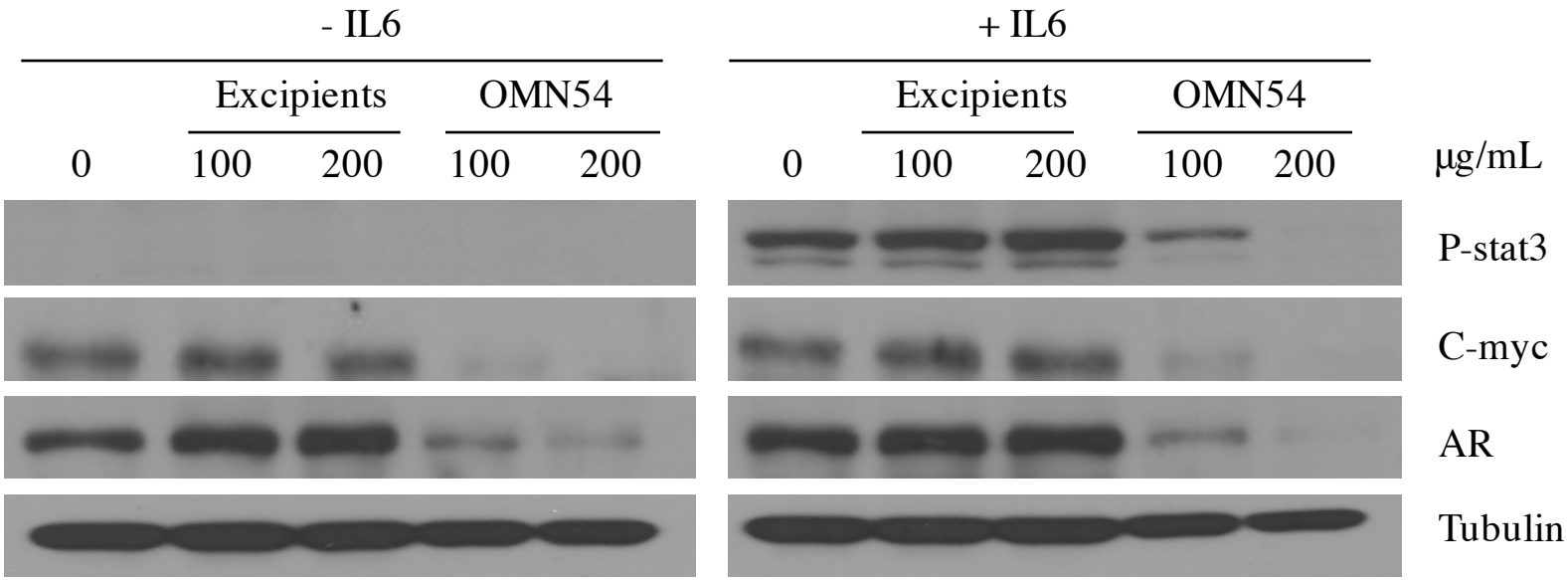
Human Primary Prostate Cancer (1/4 of biopsy)
Many different types of cells and at various stages of cancer development co-exist in patient tumors

Aneustat™ Multitargeted Activity Affects a Multiplicity of Signaling Pathways in Prostate Cancer Cells

Growth factor-induced AR signaling



Aneustat™(OMN54) Inhibits P-stat3, C-myc and AR—Important Targets for Prostate Cancer

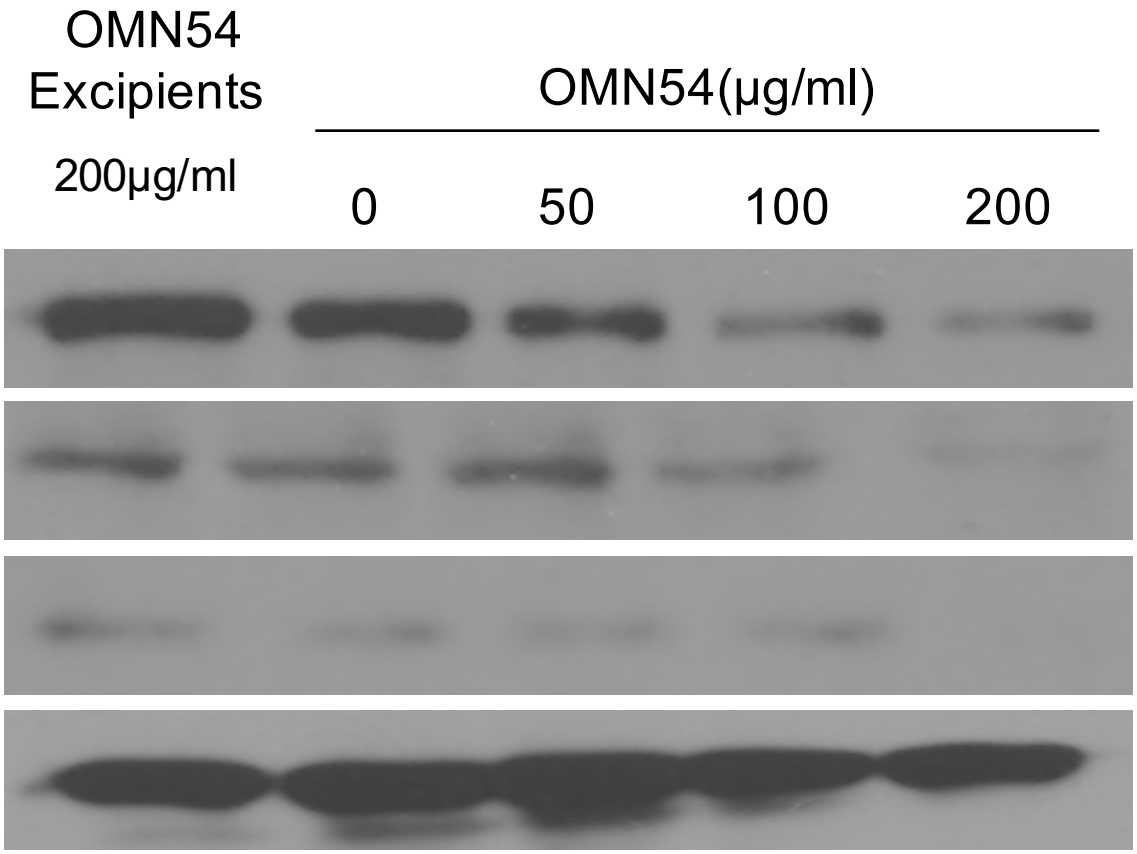


C4-2 cells *in vitro* treated over night with OMN54 in Fetal Bovine Serum (FBS) condition, then treated with 10 ng/ml IL-6 or without IL-6 for 30 minutes. Whole cell extracts were used for Western blot analysis.

Excipients: Inert substances used in Aneustat formulation

Lab: Urologic Research, Prostate Cancer Program,
UC Davis Comprehensive Cancer Center

Aneustat™(OMN54) Inhibits AR, P-AKT and BCL2—Important Targets for Prostate Cancer



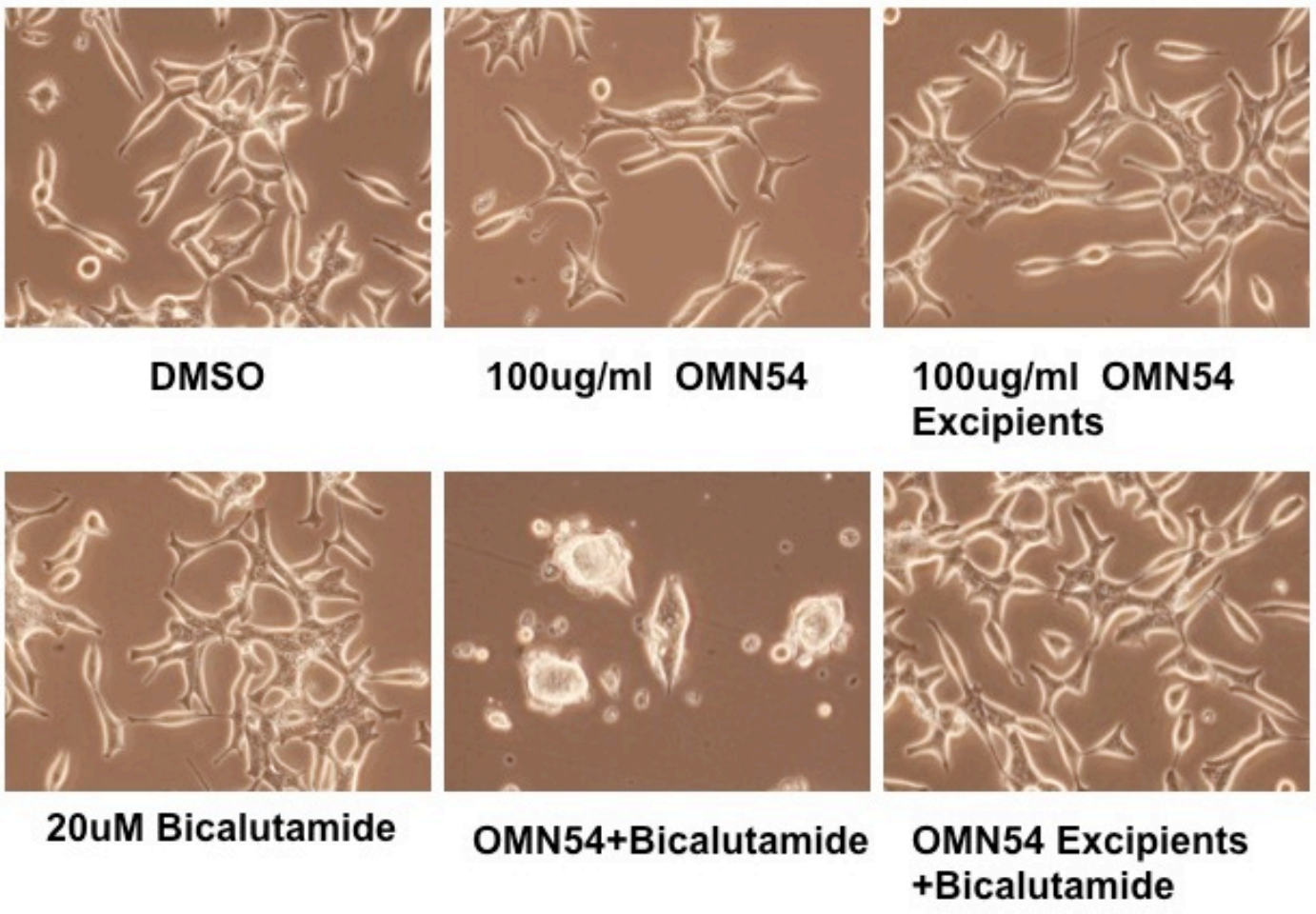
C4-2 cells *in vitro* treated with OMN54 over night in Fetal Bovine Serum (FBS) Condition. Whole cell extracts were used for Western blot analysis.

OMN54 Excipients: Inert substances in Aneustat formulation

Lab: Urologic Research, Prostate Cancer Program, UC Davis Comprehensive Cancer Center

Qu S et al; MOL ONC 8 (2014) 311-322

Aneustat™(OMN54) Accelerates Apoptosis (Cell Death) in Bicalutamide-Treated Prostate Cancer Cells (LNCaP)

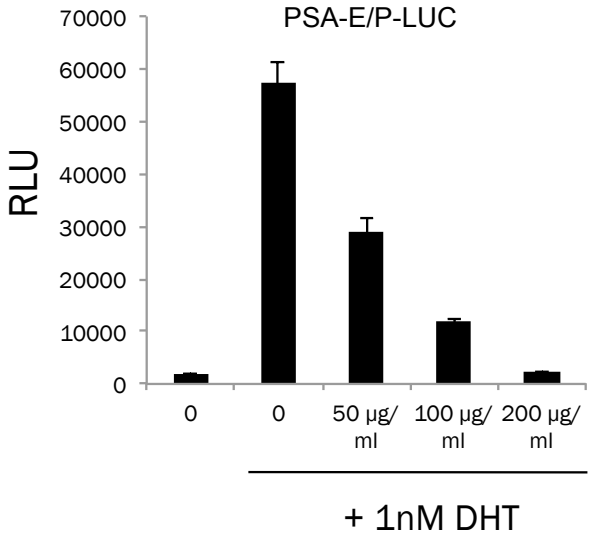


LNCaP androgen sensitive prostate cancer cells *in vitro* were treated with OMN54 and bicalutamide either alone or combination for 48 hr. These pictures show that the combination of OMN54 and bicalutamide accelerates apoptosis, while OMN54 alone mostly inhibits cell proliferation, while bicalutamide has no effect on LNCaP androgen sensitive prostate cancer cells.

OMN54 Excipients: inert substances used in Aneustat (OMN54) formulation

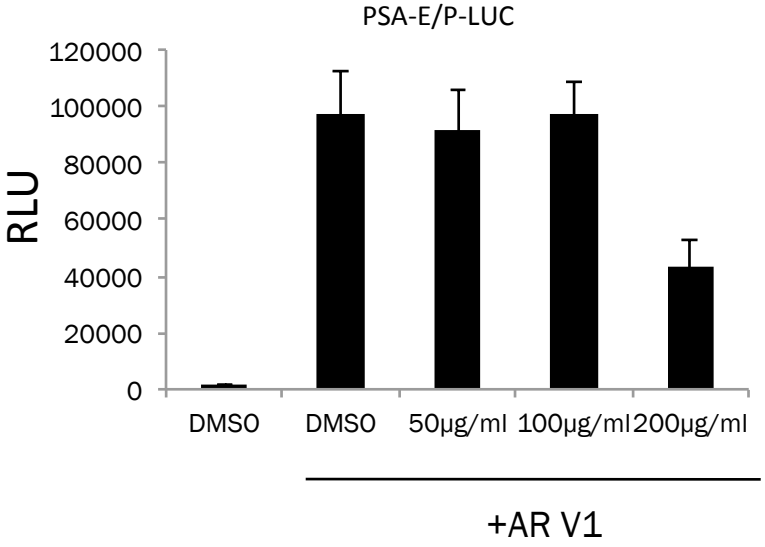
Lab: Urologic Research, Prostate Cancer Program, UC Davis Comprehensive Cancer Center

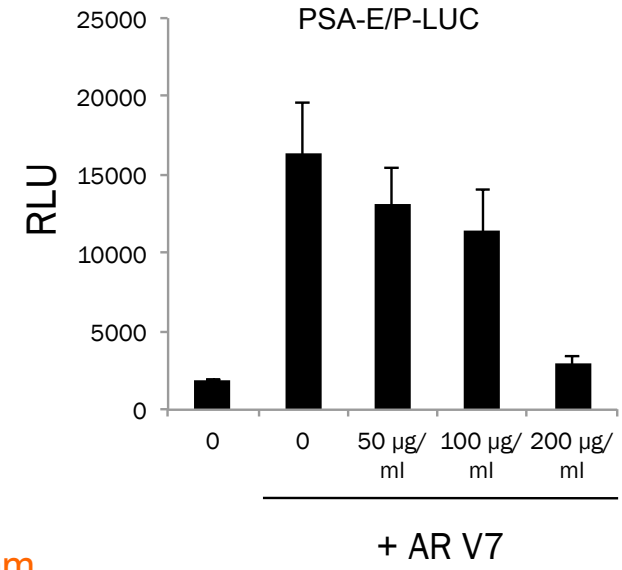
Aneustat™(OMN54) Inhibits AR Full-Length and AR Variants Mediated Transactivity in LNCaP Androgen Sensitive Cells In Vitro



LNCaP cells were co-transfected with PSA-E/P-Luc and AR-FL or AR-V1 or AR-v7, the cells were treated over night with different doses of OMN54. Cell lysates were used for luciferase activity assay.

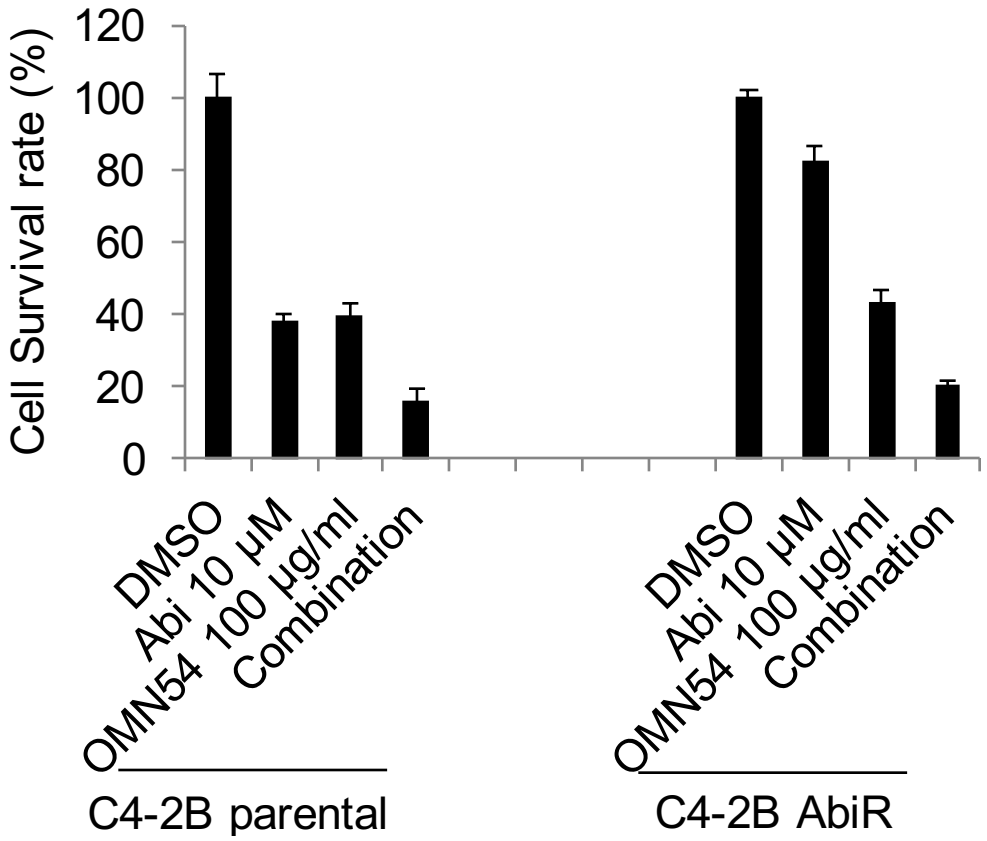
Ref: Mol Cancer Ther; 12(8) Aug 2013





Lab: Urologic Research, Prostate Cancer Program, UC Davis Comprehensive Cancer Center

Combination Treatment of Aneustat™(OMN54) With Abiraterone Demonstrates Synergistic Inhibition of Proliferation of Prostate Cancer Cells



C4-2B cells and C4-2B AbiR (abiraterone resistant C4-2B cells) were treated *in vitro* for 48 hours with either abiraterone (Abi) alone, OMN54 alone, or in combination, and then cells were counted.

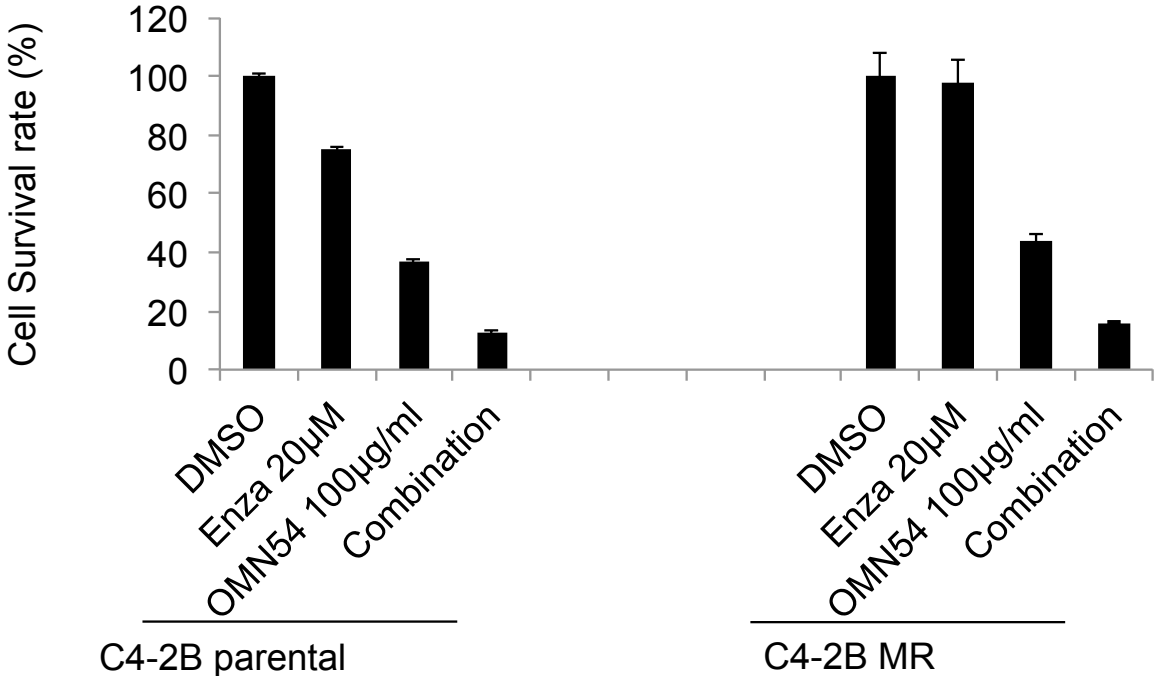
Combination:
10 µM abiraterone +
100 µg/ml OMN54

C4-2B parental: castration resistant prostate cancer cells
C4-2BAbiR: abiraterone-resistant castration resistant prostate cancer cells

Conclusion: The results show that OMN54 inhibits the proliferation of castration resistant prostate cancer cells (C4-2b) and abiraterone-resistant castration resistant prostate cancer cells (C4-2B AbiR). The combination of OMN54 with abiraterone demonstrates synergistic anti-cancer effect.

Lab: Urologic Research, Prostate Cancer Program,
UC Davis Comprehensive Cancer Center

Combination Treatment of Aneustat™(OMN54) With Enzalutamide Demonstrates Synergistic Inhibition of Proliferation of Prostate Cancer Cells



C4-2B cells and C4-2BMR (enzalutamide-resistant C4-2B cells) were treated *in vitro* for 48 hours with either enzalutamide (Enza) alone, OMN54 alone, or in combination, and then cells were counted.

Combination:
20 μM Enzalutamide +
100 μg/ml OMN54

C4-2B: castration resistant prostate cancer cells
C4-2BMR: enzalutamide-resistant castration resistant prostate cancer cells

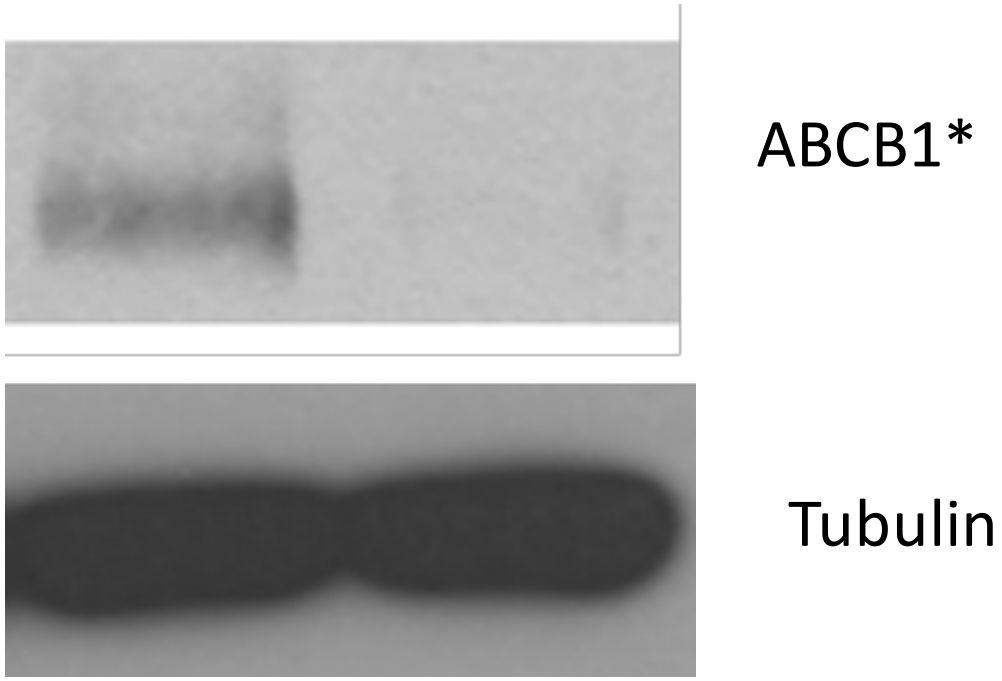
Conclusions: The results show that OMN54 inhibits the proliferation of castration-resistant prostate cancer cells (C4-2B) as well as enzalutamide-resistant castration resistant prostate cancer cells (C4-2BMR). The combination of OMN54 with enzalutamide demonstrates synergistic anti-cancer effect.

Lab: Urologic Research, Prostate Cancer Program,
UC Davis Comprehensive Cancer Center

Aneustat™(OMN54) Down Regulates ABCB1 in TAXR Docetaxel Resistant Prostate Cancer Cells In Vitro

DMSO

OMN54 (100mg/mL)



ABCB1*

Tubulin

Docetaxel-resistant and castration-resistant TaxR cells were treated with OMN54 overnight.

Cell lysates were collected for Western blot analysis. Tubulin was used as a loading control.

This data provides a mechanistic explanation for Aneustat's ability to impede the development of docetaxel resistance in prostate cancer[1].

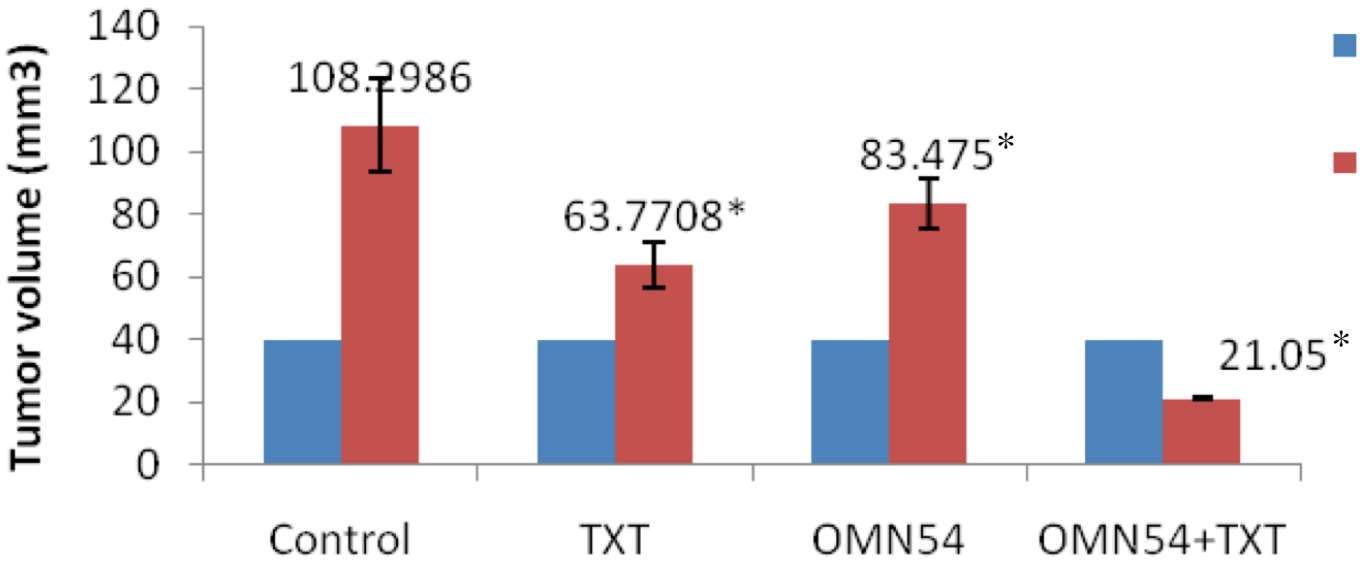
*ABCB1 protein functions as a drug efflux pump to remove toxic chemicals and chemotherapies from cancer cells. It is also know as P-glycoprotein or multidrug resistance protein 1 (MDR1).

1. Mol Cancer Ther. 2013 Sep;12(9):1829-36.

Lab: Urologic Research, Prostate Cancer Program, UC Davis Comprehensive Cancer Center

Aneustat™ Demonstrates Synergy with Docetaxel and Prostate Cancer Tumor Shrinkage In Vivo

- **BC Cancer Agency research showed that after 3 weeks of treatment, Aneustat (OMN54) in combination with docetaxel, demonstrated synergy and tumor shrinkage when treating LTL-313 (androgen-dependent; adenocarcinoma) human prostate cancer tumors SRCX *in vivo* (mice)**



Delivery Route/Dose/Frequency	
Aneustat	Taxotere (docetaxel)
oral gavage;1652mg /kg; QD x 21	IP; 5 mg/kg/QD; d 2, 9, 16

** p<0.05 relative to control*

Qu S et al; MOL ONC 8 (2014) 311-322

Aneustat™ in Combination with Docetaxel Synergistically Modulates Multiple Pathways Associated with Cancer (Ingenuity Pathway Analysis of DNA Microarray Data) Human Prostate Tumor In Vivo

Pathways	Aneustat™	docetaxel	Aneustat™+docetaxel
LXR/RXR Activation	↑	–	↑
Serotonin Degradation	↑	–	–
GADD45 Signaling	↑	↑	↑
p53 Signaling	↑	↑	↑
Cyclins and Cell Cycle Regulation	↓	↓	↓
cAMP-mediated Signaling	↓	↓	↓
G-Protein Coupled Receptor Signaling	↓	↓	↓
Cell Cycle: G1/S Checkpoint Regulation	↓	↓	↓
Mitochondrial Dysfunction	↓	↓	↓
IL-8 Signaling	↓	↓	↓
Mechanisms of Cancer	–	↓	↓
Mitotic Roles of Polo-like Kinase	–	–	↓
Cell Cycle Control of Chromosomal Replication	–	–	↓
ATM Signaling	–	–	↓
Role of CHK Proteins in Cell Cycle Checkpoint Control	–	–	↓
Cholesterol Biosynthesis	–	–	↓
Glycolysis I	–	–	↓
Gluconeogenesis I	–		↓

Proliferation Metabolism ↓=inhibited; ↑=stimulated

Qu S et al; MOL ONC 8 (2014) 311-322

Aneustat™ in Combination with Docetaxel Synergistically Modulates Multiple Genes Associated with Cancer Hallmarks: Sustaining Proliferative Signaling Human Prostate Tumor In Vivo

Associated Cancer Hallmark: Sustaining Proliferative Signaling

Gene ID	Aneustat	docetaxel	Combo
MKI67	-1.60	-1.11	-4.83
SMC4	-1.77	-1.14	-4.22
CDC7	-1.44	-1.12	-4.53
MCM10	-1.70	-1.13	-12.52
FOXM1	-1.59	-1.08	-7.47
UBE2C	-1.48	-1.02	-9.43
CDKN3	-1.57	-1.10	-7.83
KIF4A	-1.55	-1.07	-8.71
EXO1	-1.36	-1.15	-8.94
DTL	-1.65	-1.16	-9.69
TOP2A	-1.46	1.08	-8.18
PLK1	-1.36	1.03	-5.75
SGOL1	-2.18	-1.09	-7.64
CASC5	-2.17	-1.06	-9.61
CEP55	-1.64	-1.15	-8.60
DLGAP5	-1.82	-1.14	-8.36
KIF20A	-1.69	-1.04	-10.44
NUF2	-1.75	-1.11	-8.24
BUB1	-1.86	-1.15	-8.22
KIF23	-1.55	-1.09	-4.57
TACC3	-1.66	-1.17	-7.88
CENPE	-1.74	-1.04	-7.87

Gene ID	Aneustat	docetaxel	Combo
RAD54L	-1.86	-1.31	-7.84
UHRF1	-1.91	-1.59	-6.79
SPC24	-1.44	-1.07	-7.51
KIF14	-1.89	-1.23	-7.42
CENPA	-1.71	1.04	-7.99
E2F2	-1.61	-1.15	-6.99
FANCA	-1.64	-1.18	-6.18
BMP6	-1.50	1.08	-3.48
ANLN	-1.65	-1.24	-10.71
BLM	-1.57	-1.10	-4.40
TONSL	-1.75	1.02	-4.76
AMOT	-1.68	-1.19	-3.67
AURKA	-1.51	1.03	-3.58
OXGR1	-1.84	-4.28	-3.93
CDT1	-1.74	-1.24	-5.98
SPC25	-1.36	-1.26	-5.61
POLQ	-1.65	-1.05	-5.52
SKA2	-1.15	1.07	-3.67
ORC1	-1.30	-1.12	-4.94
SPAG5	-1.68	-1.18	-4.76
INSIG1	-1.88	-1.62	-4.73
NEK2	-1.87	-1.07	-4.71
SKP2	-1.22	-1.26	-2.48

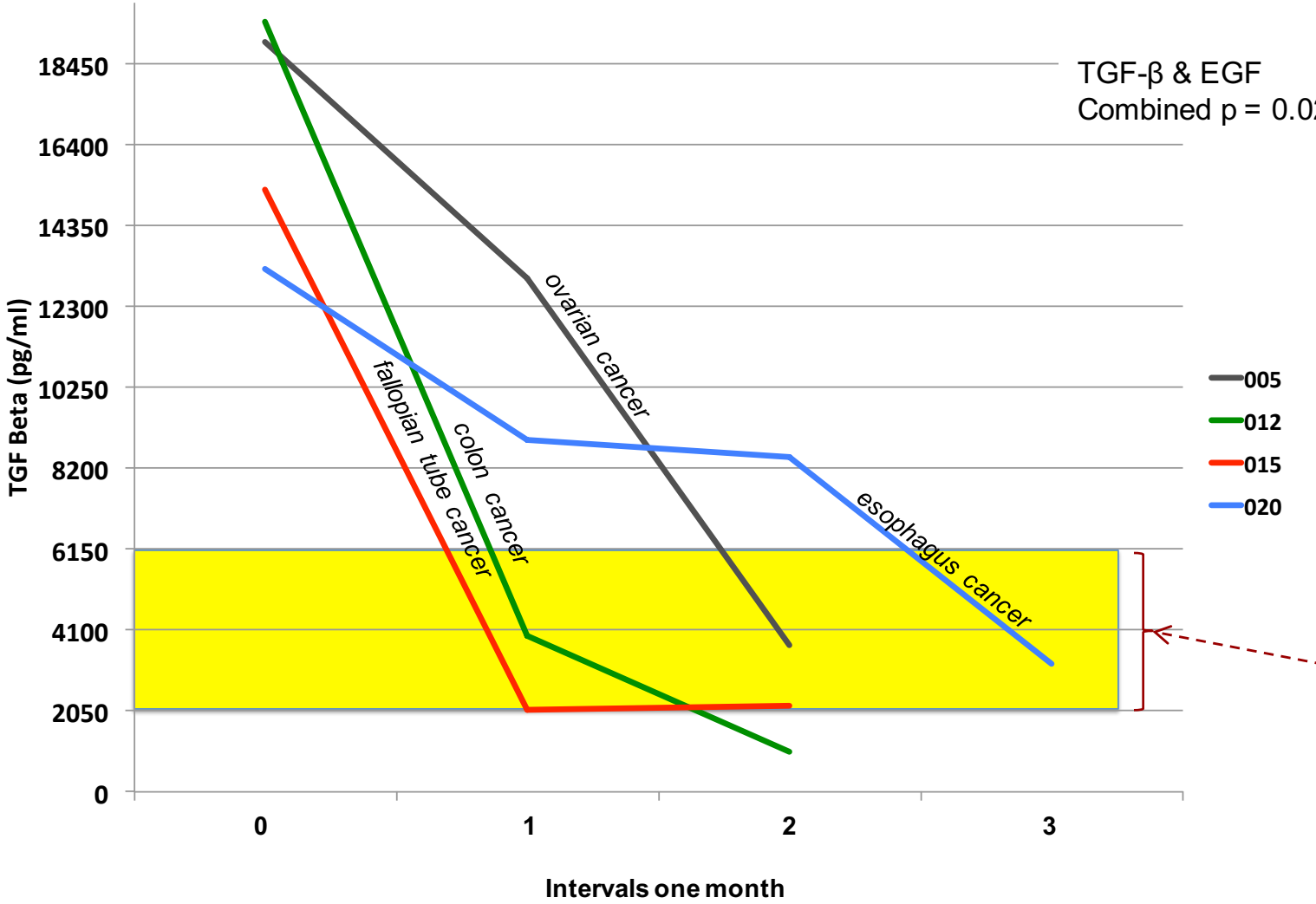
Qu S et al; MOL ONC 8 (2014) 311-322

Aneustat™ (OMN54) Phase I Clinical Trial Summary of Results

- **Trial conducted at BC Cancer Agency Vancouver, BC, Canada**
- **No documented toxicity or significant side effects attributed to therapy**
- **Good subject quality of life and compliance with therapy**
- **No accumulation of parent compounds (t1/2<2 hours)**
- **Preliminary indication of therapeutic activity**
  - Dose responsive reduction in TGF-β, EGF, and Rantes, biomarkers of immune suppression and cancer promoting activity
  - Maximum therapeutic exposure—8 months

TGF-β Levels in Plasma From Subjects in Aneustat™ Phase I Clinical Trial

Subjects with most abnormal TGF-β values at study entry



TGF-β & EGF
Combined p = 0.029

Notes:
005-Sample 1: 40271
012-Sample 1: 23066

Patient	Daily Dose	Primary Tumor Type
005	2gm QD	ovarian
012	1.5gm BID	colon
015	2gm BID	fallopian tube
020	2.5gm BID	esophagus

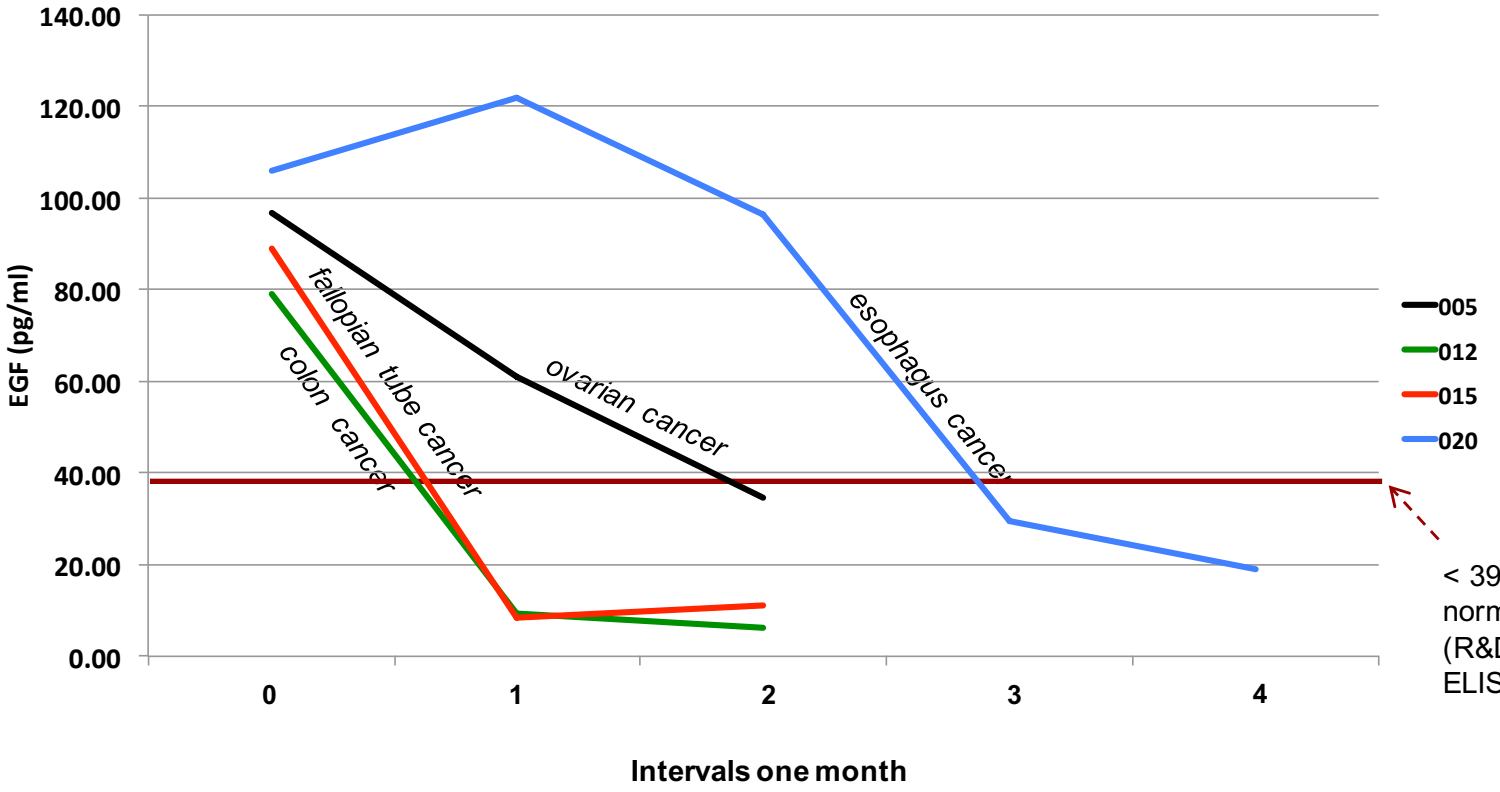
TGFβ range
(+/- 1 Standard Deviation)
in healthy people[1]

1. Wakefield et al, Clin Cancer Res. 1995 Jan;1(1) 129-136

EGF Levels in Plasma From Subjects in Aneustat™ Phase I Clinical Trial

Subjects with most abnormal EGF values at study entry

TGF-β & EGF
Combined p = 0.029



Patient	Daily Dose	Primary Tumor Type
005	2gm QD	ovarian
012	1.5gm BID	colon
015	2gm BID	fallopian tube
020	2.5gm BID	esophagus

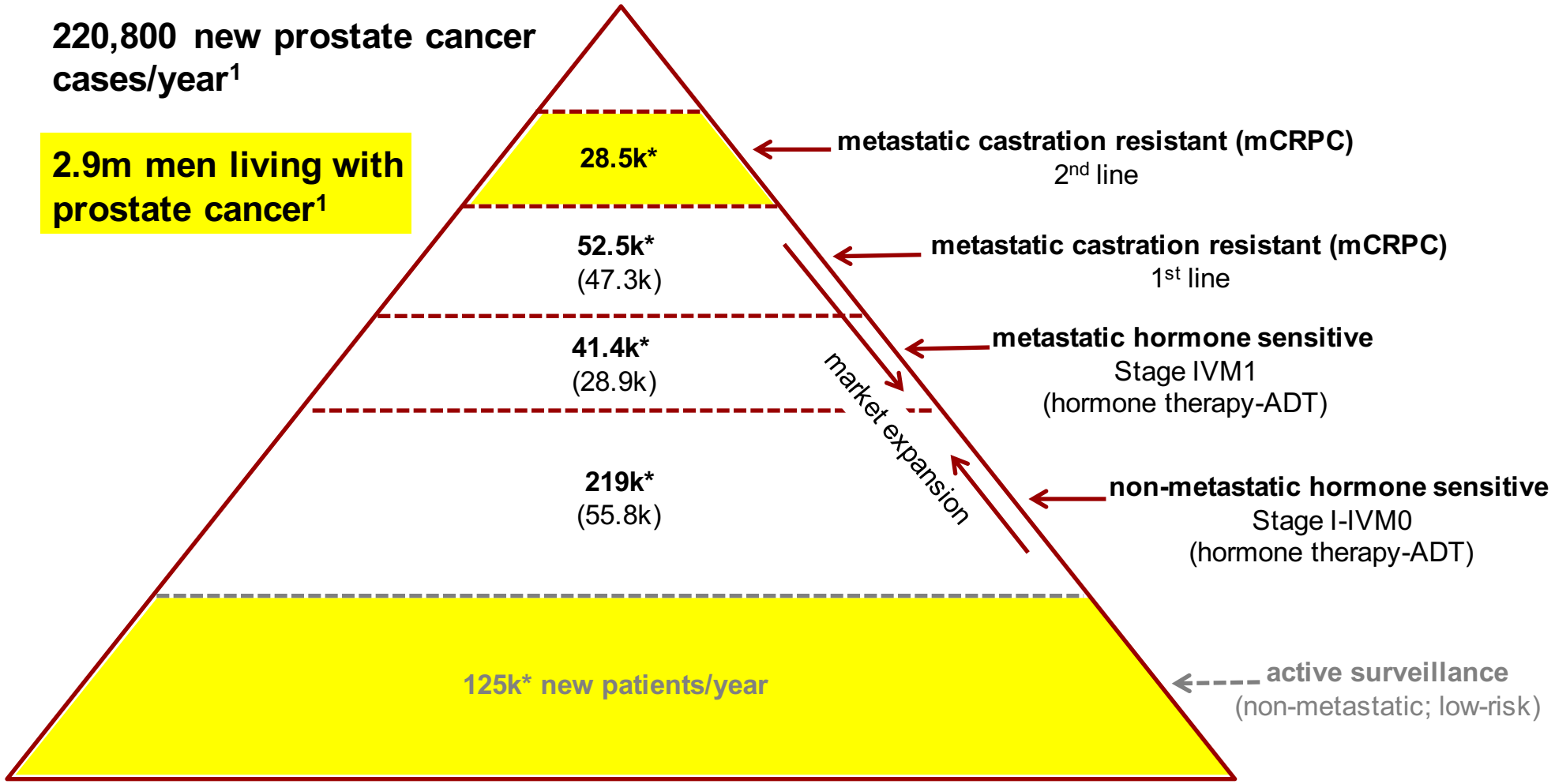
Aneustat™ Potential Ubiquitous Application to Intercept, Treat, and Prevent Cancer and Co-Existing Diseases to Reduce Disease Incidence and Healthcare Cost

Clinical Strategy	Cancer Interception		Treat/Prevent Metastasis Prevent Recurrence			
Target Organ	Chronic Benign Diseases ⇏	Pre-Cancerous Condition ⇏	Early Stage Cancer **X**	Late Stage Cancer **X** in combination with other standard of care		
Prostate	**X** BPH Prostatitis	**X** PIN/PIA	Active Surveillance	**X** Standard of care for Chemo-Naïve mCRPC/adjuvant	Standard of Care for Chemo or AR refractory mCRPC	**X** Treatment for triple-refractory mCRPC
Breast	**X** Chronic Inflammation (dense breasts)	**X** Atypical DH BRCA1&2 Family History	Post initial curative surgery DCIS	**X** Standard of care for Chemo-Naïve/adjuvant	Standard of care for previously treated	**X** Standard of care for refractory
Pancreas	**X** Diabetes And Pancreatitis	**X** Family history and predictive genetics IPMN	progression after initial radical surgery	**X** Standard of care for Chemo-Naïve/adjuvant	**X** Standard of care for previously treated	**X** Standard of care for refractory
Lung	**X** COPD	High risk population	**X** Post radical surgery progression	**X** Standard of care for Chemo-Naïve/adjuvant	**X** Standard of care for previously treated	**X** Standard of care for refractory
Colon	**X** IBD	**X** FAP HNPCC	progression after curative surgery for localized disease	**X** Standard of care for Chemo-Naïve/adjuvant	Standard of care for previously treated	**X** Standard of care for refractory
Liver	**X** Cirrhosis	**X** HBV HCV	progression after initial surgical resection	**X** Standard of care for Chemo-Naïve/adjuvant	**X** Standard of care for previously treated	**X** Standard of care for refractory

Initial company clinical development (2015)

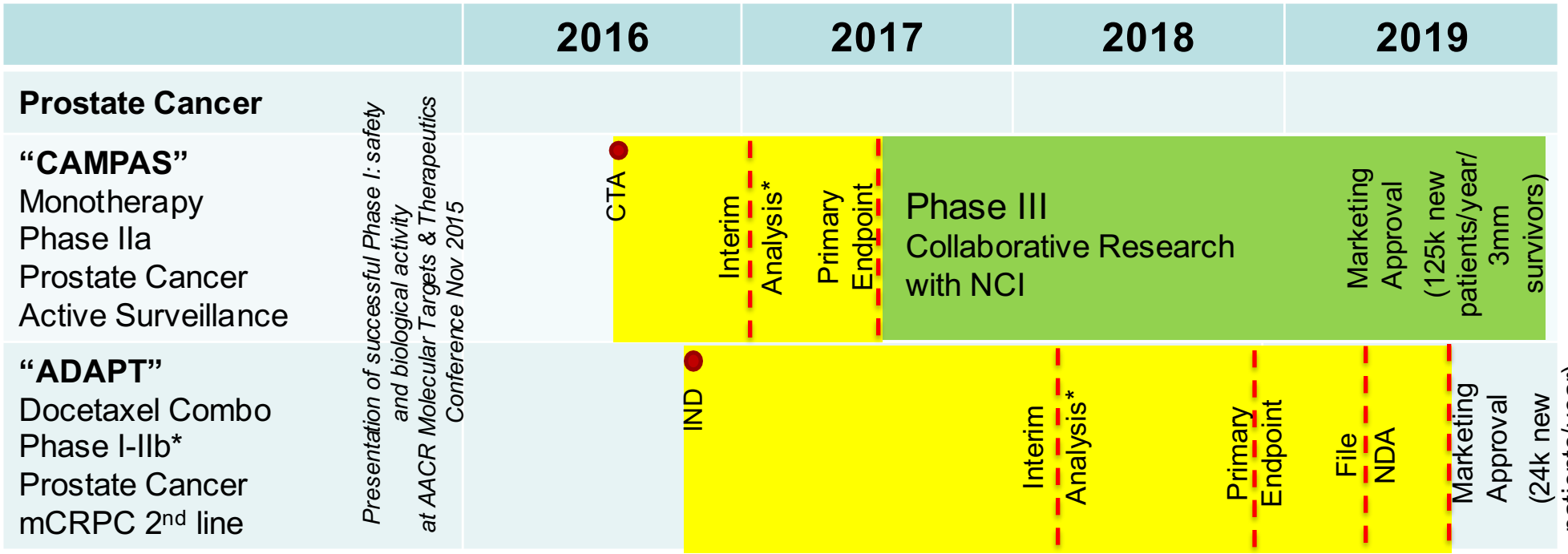
R&D partnership projects with cancer foundations (in discussions)

Aneustat™ Prostate Cancer U.S. Market Initial Opportunities: Early➔Late Stage Disease



**addressable market in U.S.*
(estimated population selecting drug treatment)
IMS Health: Disease Insights
1. American Cancer Society

Aneustat™ Clinical Trial & Marketing Approval Goals to Meet Unmet Needs in Oncology in U.S. & Canada (Feb 2016)



*randomized double blind placebo control trial

Omnitura Funding

NCI Funding

*opportunity for stimulating pharma partner collaborations

Aneustat™– An Improved Pharmacological Paradigm the SMART Platform for Combination Therapy for Cancer

Systems Diagnosis

Analyze
- Genetic mutation (gene sequencing)
- Chronic disease information status (biomarker)

Characterize
- Validate single function mutation
- Extent of activation of chronic disease engine

Rational Patient Stratification

Stratify patient with:
- Improved and more complete knowledge
- Precision targets identified due to improved signal to noise in all biological pathways

Therapy

Patient Situation		
Pre-Cancer Disease	Early Stage Cancer	Late Stage Cancer
	Local Therapies Surgery or Radiation ±Adjuvant Therapy	Single or Dual Target I.O. or Chemo

+

Aneustat™ (the SMART foundational drug)
- Master controller of all hallmarks of cancer
- Master regulator of the neuroimmune system

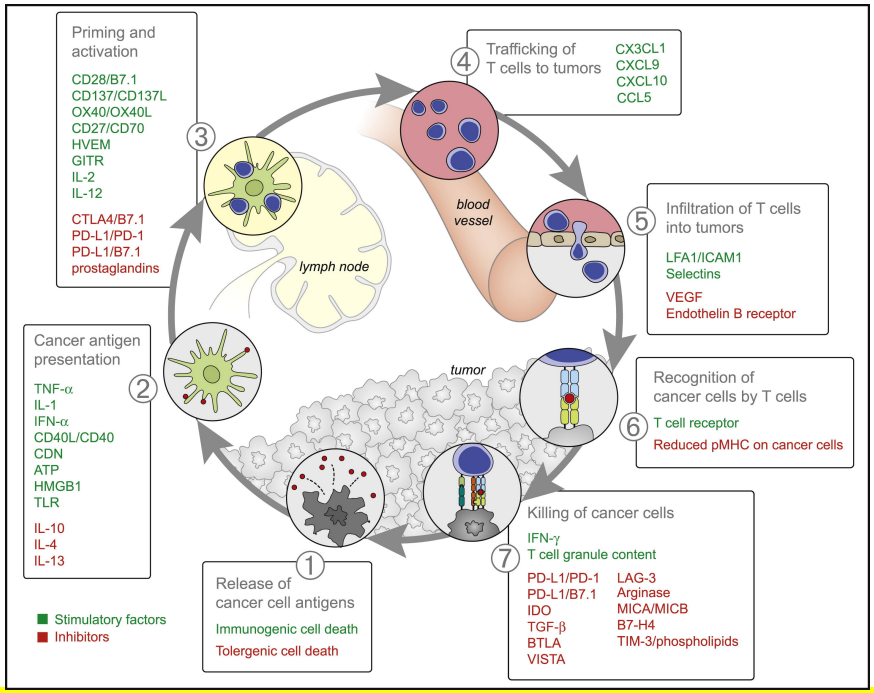
SMART™ =
S: Safe/Synergistic
M: Multivalent/Mechanism
A: Adaptive Arsenal
R: Regulation/Restoration to normal
T: Therapy/Treatment

Rationale for Combination of Checkpoint Inhibitors With Aneustat™

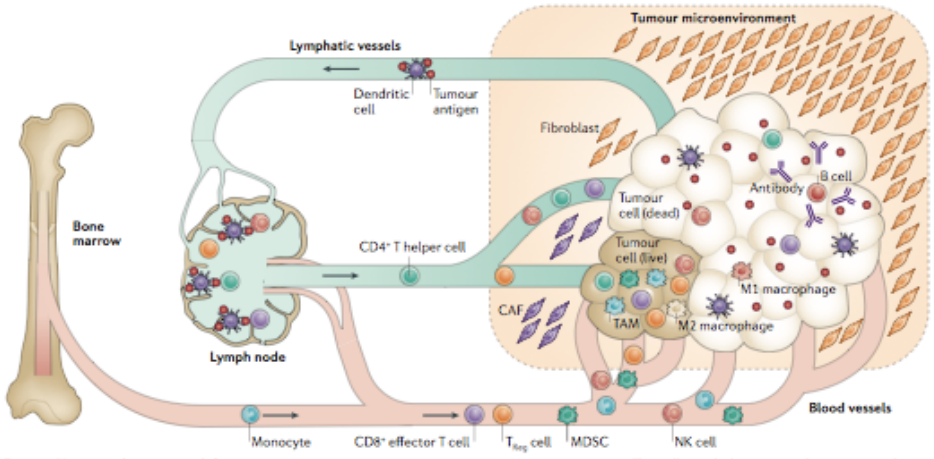
1. Checkpoint inhibitors (CPI) would work more effectively if during the course of increased immunological pharmacodynamics, the potentiation of inflammation, unchecked cellular growth and angiogenesis, unresponsiveness to growth regulating factors could be brought controlled.
2. Aneustat™ has been shown in pre-clinical and clinical testing to do the above and create immune equilibrium in a patient.
3. There is a clear rationale for synergy in combinatorial immunotherapy using Aneustat™ as the foundational drug.
4. Omnitura invites partners for R&D collaboration to improve safety and long-term efficacy while minimizing side effects and drug resistance for patients, thus reducing clinical trial risk for single targeted checkpoint inhibitors and next generation targeted immune therapies.

Aneustat™ has Promise as the Ideal Foundational Drug for Cancer, Neurodegenerative and Autoimmune Diseases

Immune response to cancer is altered by the tumor microenvironment



Aneustat:
Promotes balance between immunity stimulating and inhibitory factors

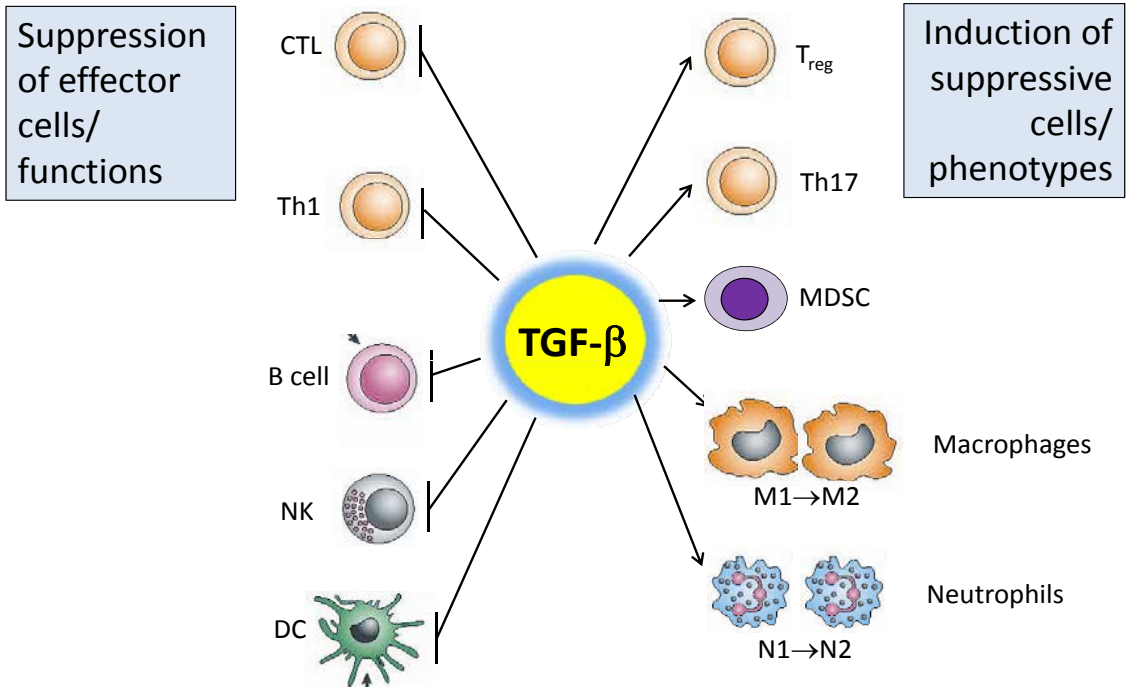


Aneustat:
- Promotes effector microenvironment
- Prevents suppressive microenvironment

Adapted from: Oncology Meets Immunology: The Cancer-Immunity Cycle, Chen, Daniel S. et al. 2013, Immunity, Volume 39 , Issue 1 , 1 - 10

TGF-β Affects Many Cells in The Immune System

Cellular targets of TGF-β-driven immune suppression



Normal level of TGF-β is a **good soldier** promoting the survival of effector cells

Immune system in equilibrium

Elevated TGF-β is a **bad general** in promoting cancer

Immune system out of equilibrium

Modulation of TGF-β Expression Plays a Role in the Pathogenesis of Many Human Diseases

- Perturbations in the TGF-β pathway are a feature of many pathological states, such as **CANCER**, *neurodegeneration and autoimmunity*[1,2]
- **TGF-β** is a key immune regulatory cytokine in maintaining immune equilibrium, **normal TGF-β levels** favor anti tumor immunity[3]
- **Normal level of TGF-β** is essential for survival of memory T cells against tumor antigens[3]
- **Elevated TGF-β levels** result in the loss of anti tumor immunity and are present in many advanced tumors[4]
- ***Increased circulating TGF-β*** is a biomarker of advancing disease and high expression is correlated with metastasis and prognostic of aggressive disease, *e.g. (i) Glioblastoma malignancy[5], (ii) Prostate cancers with the highest bone metastatic burden*[6]

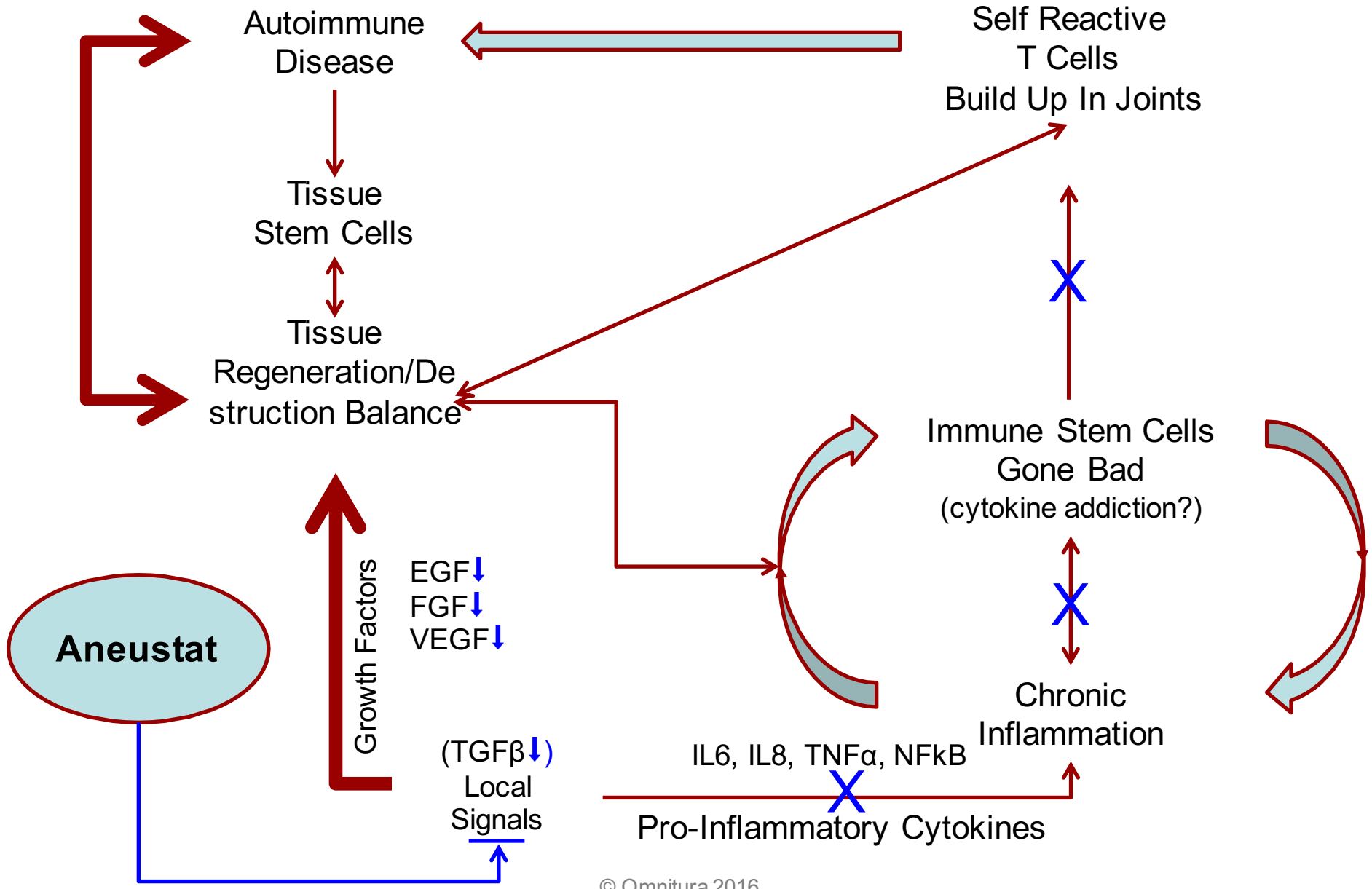
1.) Akhurst RJ & Hata A Nat. Rev. Drug Discovery 2012 11:790-811
2.) Derynck R & Akhurst R Nature Cell Biology 2007 9, 1000-1004
3.) Ma and Zhang PNAS 2015: 112(35) 11013-11017
4.) Neuzillet C. et. al. Pharmacology and Therapeutics 2015 147:22-31
5.) Han J et. Al. Amer J. Cancer Res 2015 5(3) 945-955
6.) Jones E, et. Al Expert Opinion: Therapeutic Targets 2009 Feb 13 (2) 227

Aneustat™ vs Other TGF-β Blocker Type Drugs for Treating Perturbations in TGF-β Pathway

- Normal levels TGF-β is an **immuno-regulatory** cytokine involved in maintaining **immune equilibrium** and coordinating responses to injury and stress[1]
- **High levels of TGF-β** induce high levels of regulatory T cells (Treg) which block anti-tumor immunity[2]
- **Current small molecule TGF-β inhibitors** block specific TGF-β activity or expression which cause immune dysfunction and dangerous hyper immune response in patients
- **Aneustat will reduce elevated TGF-β to normal levels, but will not affect normal TGF-β expression required for immune equilibrium, thus creating synergy with checkpoint inhibitors – improve safety and efficacy while minimize side effects and drug resistance**

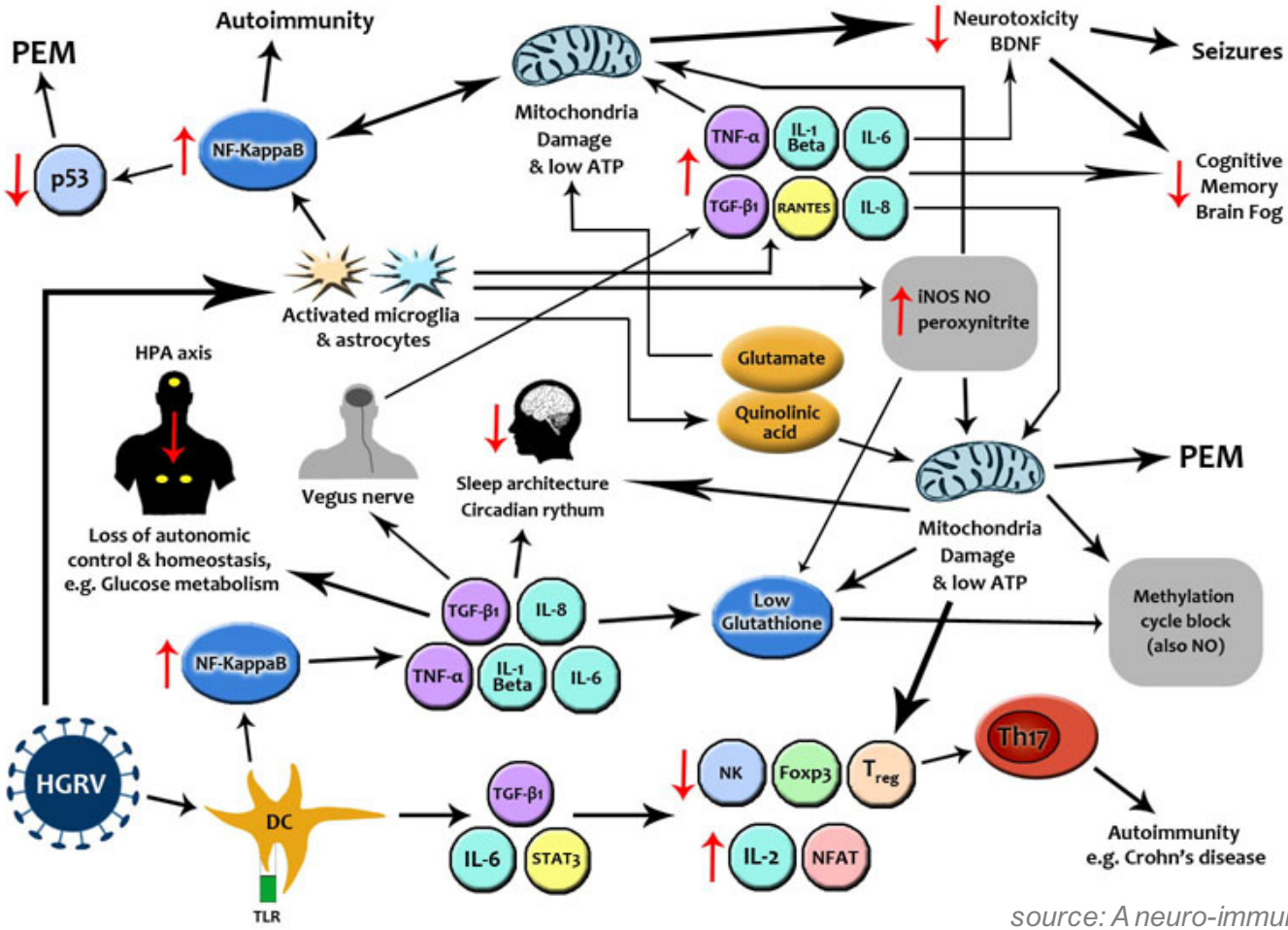
1.) Derynck R & Akhurst R Nature Cell Biology 2007 9, 1000-1004
2.) Zhang et al Am. J Cancer Res. 2015 June 15:5(7) 2190

Aneustat™ Simultaneously Regulating Multiple Immune Signaling Pathways Could Prevent & Treat Chronic Diseases Including Cancer



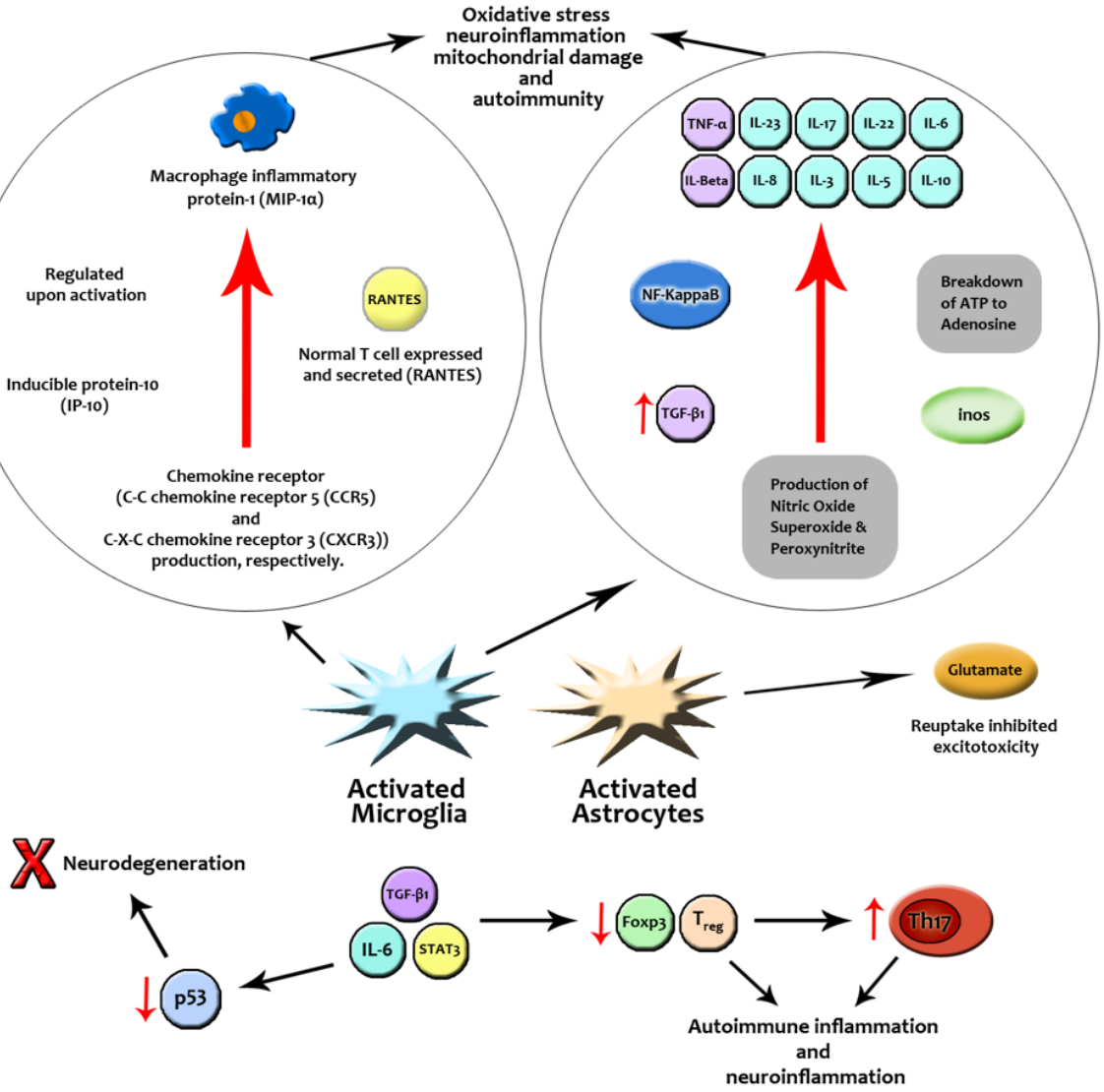
Aneustat™ can Also Treat Co-Existing Diseases in Cancer Patients

Aneustat™ promotes immune equilibrium in pathways shared by autoimmune and neurodegenerative diseases



source: A neuro-immune model of Myalgic Encephalomyelitis/Chronic fatigue syndrome; Morris & Maes; Metab Brain Dis. 2012 Jun 21

Oxidative Stress and Mitochondrial Damage in Autoimmune and Neuroimmune Disease



source: A neuro-immune model of Myalgic Encephalomyelitis/Chronic fatigue syndrome; Morris & Maes; Metab Brain Dis. 2012 Jun 21

Genyous Biomed has a Platform of Proprietary Multivalent Compounds to Treat Heterogeneous Autoimmune and Neurodegenerative Diseases

- Remove performance barriers of current drugs to intercept, treat, and prevent recurrence of chronic diseases, reduce disease incidence for patients and economic burden for patients and society.
- Increase safety and long-term efficacy to manage specific or co-existing chronic diseases
- Reduce side effects and morbidity and to improve patient productivity
- Create synergistic combinations with current standard of care therapies, legacy drugs, and next generation targeted drugs
- These new combinations could also be patentable block buster drug candidates
- Current opportunities include preclinical to phase II/III clinical development for rheumatoid arthritis, cystic fibrosis, Crohn's disease, multiple sclerosis, chronic fatigue syndrome, autism, Alzheimer's and Parkinson's.
- Genyous Biomed invites collaborators for joint R&D to accelerate a new medical paradigm for treating heterogeneous autoimmune and neurodegenerative diseases.

Summary of Meeting With Merck

- **Omnitura invites Merck to make immediate investment $10mm to accelerate clinical development of Aneustat™ and to gain the first right to negotiate for licensing Aneustat™**
- **Omnitura invites Merck to perform due diligence towards licensing and joint phase IIb development of Aneustat™**
- **Omnitura invites Merck to enter into R&D to test combination I.O.: Aneustat™ + Keytruda**
- **Genyous Biomed invites Merck to commence separate discussion on multivalent neuroimmune therapy for autoimmune diseases and neurodegenerative diseases**