

# Bio-Modeling Systems

## The Mechanisms-Based Cosmetic Company

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We changed the discovery paradigm to create novel cosmetic meanings  
**from unreliable heterogeneous sources of data**

R&D conference Cosmetic 306  
Paris october 16-17, 2019

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# BMSystems Group description

- Independent Private Company incorporated in 2004. 100% owned by its founders.
- Profitable since 2006, thanks to our recurrent clients.
- We only sell the results of the R&D programs, not our proprietary technologies.
- 100% biology driven company focused on discovery, and critical high impact decisions making
- A unique proprietary CADI™ Knowledge Database of mechanisms & interactions.
- Not domain-dependent, but information-dependent.
- Markets: Pharma, Cosmetics, Nutrition, Health Technologies, Connected health,
- Highly productive 24 vFTE\* of which 9 vFTE on CADI™ Discovery programs only.
- Strong & long term strategic R&D collaborations (>100 people collaborating).
- Dual business model : Contractual or Collaborative R&D programs.
- External valorization of our collaborative R&D programs through out-licensing or spin-off.
- Outstanding internal pipeline of programs ready for collaborations.
- *14 successes independently validated by our clients/partners of which: 1 therapeutic spin-off and 1 exclusive out-license, 4 issued patents, 10 publications.*
- *Potential competitors: Key Opinion Leaders, dominant thinking companies or pharma Systems Biology or bioinformatics teams argue they can do the same. We are always open for discussions & comparisons on success rates and outputs for patients.*

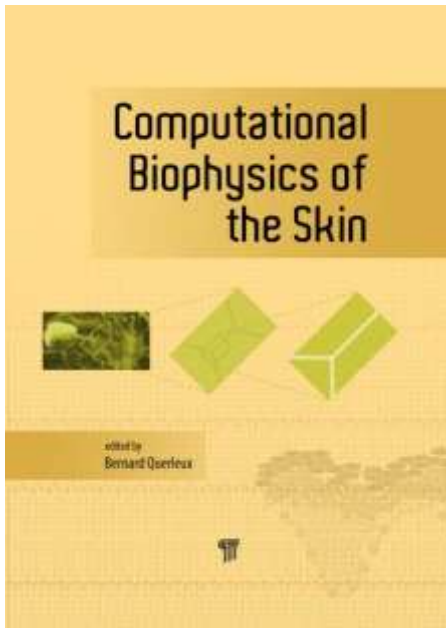
The World's first Mechanisms-Based Medicine Company  
You have a R&D issue or a decision to make, we may have a solution for you.

# “Mechanisms-Based Cosmetic”: CADI™ applied to cosmetics

1. Skincare: Strong integrated understanding of the global systems:

1. *The mechanisms associated with constitutive and facultative epidermal pigmentation*
2. *The mechanisms associated with senile/solar lentiginos (aging issues)*
3. *Components specific to pigmentation from production to destruction*
4. *Microbiota & Skin Mechanisms*

Contributor to The first reference book on “*Computational Biophysics of the Skin*” edited by Prof. Bernard Querleux , scientific chairperson of the International Society for Biophysics and Imaging of the Skin. R&I L’Oréal.



Program Name	Validation / Business Partner(s)	CADI™ compliance	CADI™ vers. 0
<b>Skin Contact Allergy Mechanisms</b>	Open		high Interest
<b>Skin pigmentation Mechanisms</b>	Open		high Interest
<b>Skin pigmentation Modulation</b>	Open	high Interest	
<b>Skin aging Mechanisms</b>	Open	high Interest	
<b>Modulation of skin hydration</b>	Open	high Interest	
<b>Modulation of the lipid constituents of the skin barrier</b>	Open	high Interest	
<b>Novel Hair Loss Mechanisms</b>	Open	high Interest	

Mechanisms-Based Cosmetic : CADI Discovery applied to cosmetics  
 A new paradigm qualified for novel solutions in premium personalized marketing strategies

# On going BMSystems' outstanding collaborative R&D programs



**Microbiota & Autism H2020 program selected for 14 M€ funding.** [GEMMA program](#) (Genome, Environment, Microbiome and Metabolome in Autism) gathers an international consortium of scientists to study the role of the gut microbiome in the development of Autism Spectrum Disorders (ASD).

**Etiology & Epigenetic for metabolic disorders program self funded.** [UMANG program](#) How does maternal nutrient restriction coupled with defective one-carbon metabolism alter the foetal development program, leading to enhanced predisposition to T2D in adolescence? Centre of excellence in Epigenetics IISER Pune India



**Diagnostic & Therapeutic evaluation program self funded.** The French Chronic Fatigue Syndrome Association [decides to clinically evaluate the ME/CFS pathogenesis model](#) produced by Bio-Modeling.



## BMSystems' outstanding POCs and our 2 first external outputs



**BMSystems/CEA collaborative research in neurodegenerative diseases.** World's first in vivo validation of the mechanisms of Creutzfeldt-Jakob disease pathogenesis & progression. Two Awards (Bio IT World Best Practice Award [2009](#) and European Commission [2010](#)).



**[Pherecydes-Pharma \(2006\): BMSystems' spin-off](#)**, (novel M.R. anti-bacterial nano-agents biotherapies), two indications: [Multi-resistant Skin infections](#) in Phase I/II. & osteo-articular infection compassionate [use success](#).



**CEA/BMSystems [collaborative research in CNS](#)** (psychiatric and neurological disorders) led to the [co-owned patent WO201029131](#) with [a worldwide exclusive license](#) to [Theranexus](#) CEA's spin-off currently in Phase II.

# Our solutions to address Industry critical issues

- CADI™ Discovery's ***Integrated Descriptions of Biological Systems*** is a valuable tool to generate novel hypotheses and/or challenge existing programs, key opinion leaders and experts recommendations spread all over the departments of the client's company or partner's structure.

We propose to R&D & Translational Medicine Executives, robust alternative decision-making to de-risk, save time, costs, and novel cost-effective diagnostics/therapies for their businesses.

1. GO-NO GO decision before product acquisition or for portfolio risk analysis.
2. GO-NO GO decision before next development phase.
3. R&D program Rescue for a program facing critical issues during its lifetime.
4. External R&D "B plan" program when the "A plan" cannot be rescued.
5. Exploratory Discovery program to discover novel causal mechanisms concepts.
6. Novel Hypotheses for therapeutic and/or diagnostic solutions discovery.

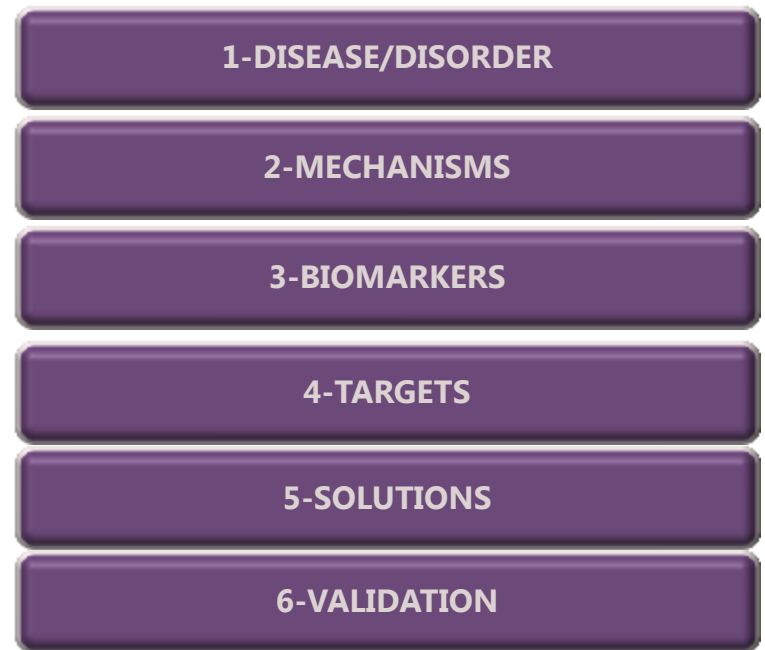
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# The Research & Development Answer

## Evidence-Based Medicine

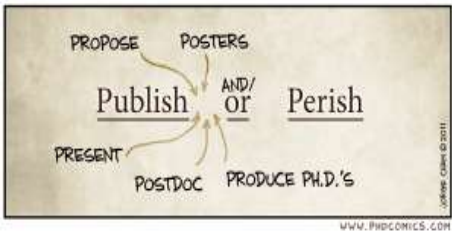
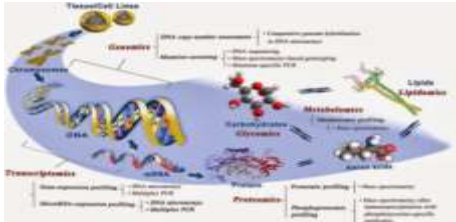


## Mechanisms-Based Medicine

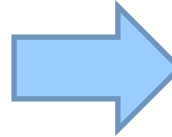


# The R&D and Real life Data Answer

To the Industry "Cartesian" answers



The  
"garbage  
in,  
garbage  
out"  
reality!



CADI Discovery Principles

- 1-Mechanisms-Based Medicine
- 2-Architectural Principle
- 3-Negative Selection Principle
- 4-4 Steps Validation Principle
- 5-Integrated Solutions Principle
- 6-The bridge R&D & Real life data



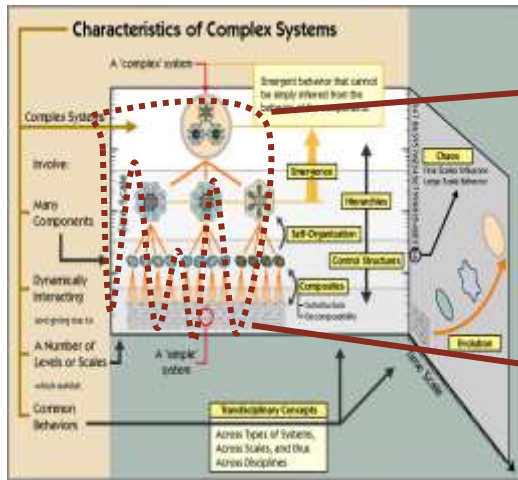
# CADI\*™ models at a glance

- CADI™ models are outstanding “non-mathematical” descriptive in-silico answers to explain the non-linear mechanisms of life and diseases.

A complex system to study

A CADI™ model representing a multiple systems in a specific context

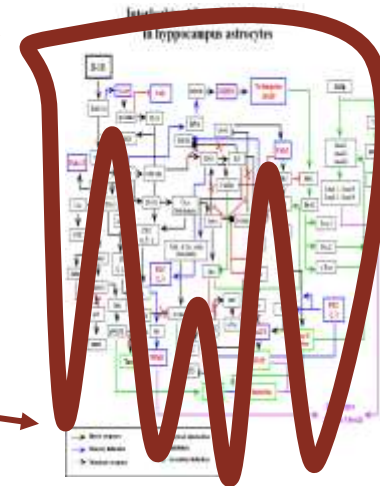
Scale / level



Different organs level

Different Cells level

Molecules level

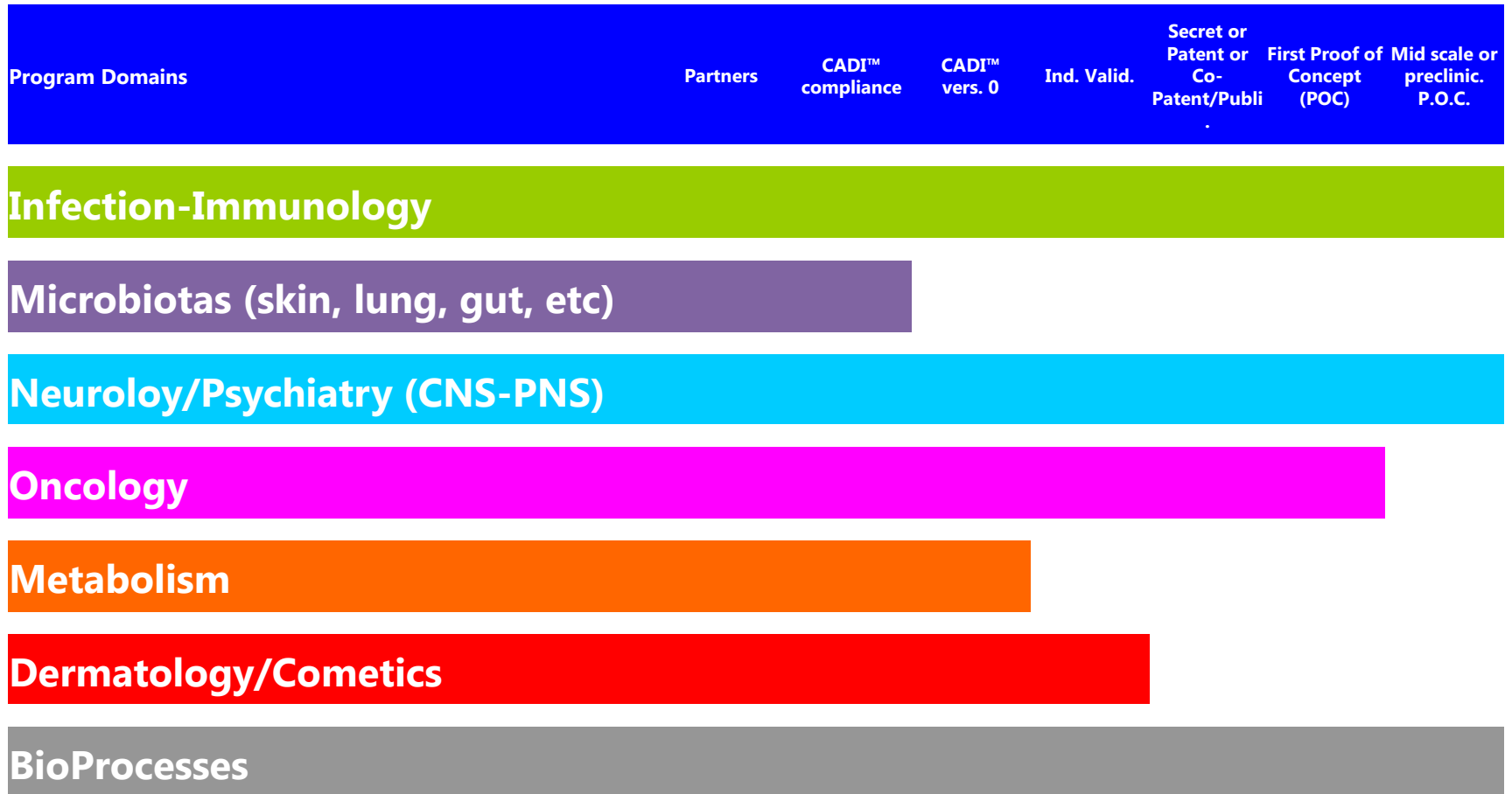


- Mathematical & Heuristic approaches can be complementary, provided they are harnessed in the proper order.

We apply first Heuristic modeling and then propose the outputs for Mathematical modeling when the system is correctly described

# BMSystems' R&D programs pipeline

External valorization of our collaborative R&D programs through out-licensing or spin-off



# BMSystems' R&D programs pipeline (details)

Program Name	Validation / Business Partner(s)	CADI™ compliance	CADI™ vers. 0	Ind. Valid.	Secret or Patent or Co-Patent/Publi.	First Proof of Concept (POC)	Mid scale or preclinic. P.O.C.
<b>Nano-Bioagents</b>	Pherecydes						Validated
TAPE (protein improvement)	Open						Validated
Chronic Fatigue Syndrome	CFS Asso			Started			
Ebola virus ecology	Open						
Hepatitis C	Open						
Auto-immune global concept	Open	high Interest					
<b>Microbiota &amp; Autism H2020 program 14 M€ funded</b>	H2020		Started				
Microbiota ecology, physiology & metabolic mechanisms	Open	high Interest					
Microbiota & inflammation	Open	high Interest					
<b>Creutzfeldt-Jakob disease's mechanisms</b>	CEA Life Sciences						Validated
Cellular & metabolic mechanisms associated with chronic anxiety	Max Planck Munich					Validated	
Psychiatric Disorders therapeutic strategy	Confidential						
Alzheimer's Disease Causal Mechanisms	Open		Produced				
Parkinson's Disease Therapy	Open		Produced				
Psychiatric inflammatory mechanisms	FondaMental Foundation		Produced				
Fibromyalgia, facial pain	Open		Produced				
Pain (Central/Peripheral)	Open		Produced				
Migraine Mechanisms	Open	high Interest					
Multiple Sclerosis Mechanisms	Open	high Interest					
<b>Etiology &amp; Epigenetic in diabetes type 2</b>	IISER Pune			Started			
Metabolic Disorders Therapy	Open	high Interest					
Hypercholesteremia Mechanisms	Open						
New global concept for Diabetes type 1	Open						
Metabolic Syndrome	Open						
<b>Breast cancer-Hras</b>	INSERM					Validated	Validated
Tamoxifen resistance	INSERM				Validated		
Specific Metastasis control	INSERM			Validated			
Encysting Tumour Therapy	Open	high Interest					
<b>Müllerian regression Mechanisms</b>	CNRS				Validated		
Adipocytes growth control	Open						
<b>Skin pigmentation Mechanisms</b>	Open			Validated			
Skin pigmentation Modulation	Open			Validated			
Skin Contact Allergy Mechanisms	Open		high Interest				
Skin aging Mechanisms	Open	high Interest					
Modulation of skin hydratation	Open	high Interest					
Modulation of the lipid constituents of the skin barrier	Open	high Interest					
Novel Hair Loss Mechanisms	Open	high Interest					
<b>Program Synthons</b>	ARD-IBT-L'Oréal						Validated
Human Glycosylation with Yeast	Open		high Interest				

# CADI™ Discovery process phases



Phase Objective	CADI™ Feasibility	CADI™ Construction	CADI™ Validation	CADI™ Exploitation
	<ul style="list-style-type: none"> <li>• 3-5 weeks</li> <li>• Identify and define what is feasible among the projects submitted.</li> <li>• Define best CADI™ modeling strategy</li> </ul>	<ul style="list-style-type: none"> <li>• Step I : 1-4 months</li> <li>• Preliminary/controls: Simulation of the whole process on a data subset before launching Step II</li> <li>• Step II: 4-10 months</li> <li>• Construction of the CADI™ models version "0" for the complete program.</li> <li>• Novel hypotheses generation</li> </ul>	<ul style="list-style-type: none"> <li>• Timing to be defined</li> <li>• Validation of the CADI™ model using the 4 steps validation process</li> <li>• Model improvement.</li> <li>• Robust hypotheses and mechanisms proposal.</li> </ul>	<ul style="list-style-type: none"> <li>• Timing to be defined</li> <li>• Proposition of robust solutions to solve client's issues.</li> <li>• Answers to the 5 client's R&amp;D and business issues.</li> <li>• Client's team exploits the Model.</li> </ul>

## Programs costs drivers

1. The company offers "one shot", "first refusal" or "post program exclusivity" deals.
2. In every case, the company offers exclusivity during the execution of the program.
3. The standard deal cost structure can be a combination of access fees, fees and success fees.
4. Domain of analysis, scope of the issues, complexity of the CADI™ model.
5. Availability and ease of access to relevant data.
6. Percentage of CADI™ knowledge database usage. In case of use of existing proprietary CADI™ programs, An additional access fees and success fees are required to compensate previous BMSystems' investments and lower risk for the clients.
7. Reactivity, readiness & willingness of the client/partner's team to contribute.

# BMSystems' CADI™ publications to date

CADI™ Models published in prestigious peer-reviewed journals: (click on the grey links to get the pdf)

- [2018: Current Opinion in Pharmacology](#): How scientific literature analysis yields innovative therapeutic hypothesis through integrative iterations. CADI Discovery addresses the complexity of life sciences mechanisms and the digital « garbage in garbage out » reality
- [2014: CNS Psychiatry publication](#): American Journal of Psychiatry and Neuroscience. Second publications with the Max Planck Institute of Psychiatry in Munich: Differential proteomics analyses reveal anxiety-associated molecular and cellular mechanisms in cingulate cortex synapses. The first output of the DECIUS CNS research program.
- [2012, CNS NEURODEGENERATIVE & PSYCHIATRY](#): PharmacoPsychiatry publishes the first review describing a productive vision of Systems Medicine that will change R&D organization and interactions between clinicians & researchers & reveals how the world's first explanation of the mechanisms of the Creutzfeldt-Jakob disease led to the discovery of a truly innovative psychiatric treatment.
- [2011, CNS PSYCHIATRY](#): Pharmaco Psychiatry publication: Proteome-Based Pathway Modelling of Psychiatric Disorders. Publication with The max Planck Institute of Psychiatry in Munich
- [2010, INFECTIOUS DISEASES](#): Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science :Genetically Engineered Virulent Phage Banks in the Detection and Control of Emergent Pathogenic Bacteria. Publication with Pherecydes-Pharma.
- [2009, TISSUE DIFFERENTIATION](#): Médecine & Sciences: Müllerian duct regression explanation. Integrative systems biology & experimental Biology. Publication with CNRS experimental data.
- [2005, CANCER](#): Journal of molecular Endocrinology: Integrative analysis of gene expression patterns predicts specific modulations of defined cell functions by estrogen and Tamoxifen in MCF7 breast cancer cells. Publication in collaboration with INSERM unit 553.
- [2003, CANCER](#): Nucleic Acids Research: Integrated transcriptome analysis of the cellular mechanisms associated with H-ras-dependent malignant transformation of the human breast epithelial MCF7 cell line. Publication in collaboration with INSERM unit 553. World first. First in-silico model of a complex human disease validated in-vitro and published.

## Collaboration to scientific reference books:

- [2014: Dermatology Cosmetics](#). The first reference book on "Computational Biophysics of the Skin" edited by Prof. Bernard Querleux , scientific chairperson of the International Society for Biophysics and Imaging of the Skin
- [2011: Phage Nano Technology](#) book published by [Valery Petrenko](#). Chapter 8: Genetically Engineered Virulent Phage Banks for the Detection and Control of Bacterial Biosecurity Threats.
- [2008: CNS: Biomarkers for Psychiatric Disorders](#). (Ref. ISBN: 978-0-387-79250-7, November 2008). Dr. François Iris, is the author of the Integrative Biology chapter of the book. The editor, Prof. Christoph W. Turck, is head of the Proteomics and Biomarkers branch at the Max Planck Institute for Psychiatry