

Bio-Modeling Systems

The Mechanisms-Based Medicine Company



Addressing the complexity of life sciences mechanisms and the digital « garbage in garbage out » reality through CADI™ Discovery for Therapeutics, Diagnostics, Nutrition, Cosmetics

“Disease-Centric” Repositioning Strategy

Repositioning Conference Medicen Findmed

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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.*
- *100% biology driven company* focused on discovery, and critical high impact decisions making.
- *A unique proprietary CADI™ Knowledge Database of mechanisms & interactions.*
- 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.
- *BMSystems values its therapeutics programs through out-licensing or spin-off.*
- Outstanding internal pipeline of programs ready for collaborations.

Our 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.

BMSystems' Business Propositions

- BMSystems Group addresses two complementary targets in Pharma, Biotech, Cosmetics, Nutrition, Bio-Production and Digital-Health businesses:
 1. *For R&D, Translational Medicine, & Digital Health Executives*, we offer robust alternative decision-making to de-risk, save time and costs of R&D and Digital Health programs,
 2. *For Business Developers, Patients Groups & Investors*, we discover novel low-risk, highly effective and cost-effective diagnostic, therapy, nutrition, cosmetic, bioprocess solutions for spin-offs or out-licensing.

- Created in 2004, profitable since 2006, thanks to our recurrent clients, CADI™ Discovery already delivered numerous operational outputs and novel businesses.

BMSystems' Partners at a glance



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): First BMSystems' therapeutic spin-off, (novel M.R. anti-bacterial nano-agents biotherapies with phages), indications: Multi-resistant infections 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 a CEA's spin-off .

BMSystems' R&D programs pipeline

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

Program Domains	Partners	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.
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Infection-Immunology

Microbiotas/Microbiome (skin, lung, gut, etc.)

Neurology/Psychiatry (CNS-PNS)

Metabolism

Cardiovascular Diseases

Oncology

Dermatology/Cosmetics

BioProcesses

Infection-Immunology	Oncology/Inflammation	Dermatology/Cosmetics
CNS-PNS/Inflammation	Tissue Differentiation	Cardiovascular Diseases
Industrial biotech/ bioprocesses	Metabolism/Inflammation	Microbiotas

BMSystems' R&D programs pipeline

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

Program Name	PROG CADI™ CODE	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 preclin. P.O.C.
Nano-Bioagents-Bacteriophages	CADI-R101	Pherecydes						Validated
TAPE (protein improvement)	CADI-R102	Open						Validated
Chronic Fatigue Syndrome / Gulf War Syndrome	CADI-R103	CFS Asso / Open			Started			
Ebola virus ecology	CADI-R104	Open						
Hepatitis C	CADI-R105	Open						
Autoimmunity : Global concept	CADI-R106	Open	high Interest					
Core symptoms of Autism mechanisms	CADI-R201	Confidential		Produced				
Microbiota & Autism H2020 program 14 M€ funded	CADI-R201	H2020		Started				
Microbiota ecology, physiology & metabolic mechanisms	CADI-R202	Open	high Interest					
Microbiota & inflammation	CADI-R203	Open	high Interest					
Creutzfeldt-Jakob disease's mechanisms	CADI-R301	CEA Life Sciences						Validated
Cellular & metabolic mechanisms associated with chronic anxiety	CADI-R302	Max Planck Munich					Validated	
Psychiatric Disorders therapeutic strategy	CADI-R303	Confidential					Ready	
Alzheimer's Disease Causal Mechanisms	CADI-R304	Open		Produced				
Parkinson's Disease Therapy	CADI-R305	Confidential		Produced				
Psychiatric inflammatory mechanisms	CADI-R306	FondaMental Foundation		Produced				
Fibromyalgia, facial pain	CADI-R307	Open		Produced				
Pain (Central/Peripheral)	CADI-R308	Open		Produced				
Migraine Mechanisms	CADI-R310	Open	high Interest					
Multiple Sclerosis Mechanisms	CADI-R311	Open	high Interest					
Etiology & Epigenetics in Diabetes type 2	CADI-R402	IISER Pune		Produced				
Metabolic Syndrome	CADI-R403	Confidential		Produced				
Hypercholesteremia Mechanisms	CADI-R404	Open						
New global concept for Diabetes type 1	CADI-R405	Open						
Metabolic Disorders	CADI-R406	Open	high Interest					
Atherosclerosis mechanisms	CADI-R901	Open		Produced				
Breast cancer-Hras	CADI-R601	INSERM					Validated	Validated
Tamoxifen resistance	CADI-R502	INSERM				Validated		
Specific Metastasis control	CADI-R503	INSERM			Validated			
Tumor Encysting Therapy	CADI-R504	Open	high Interest					
Müllerian regression Mechanisms	CADI-R601	CNRS				Validated		
Adipocytes growth control	CADI-R602	Open						
Skin pigmentation Mechanisms	CADI-R701	Open			Validated			
Skin pigmentation Modulation	CADI-R702	Open			Validated			
Skin Contact Allergy Mechanisms	CADI-R703	Open		Produced				
Skin aging Mechanisms	CADI-R704	Open	high Interest					
Modulation of skin hydratation	CADI-R705	Open	high Interest					
Modulation of the lipid constituents of the skin barrier	CADI-R706	Open	high Interest					
Novel Hair Loss Mechanisms	CADI-R707	Open	high Interest					
Program Synthons	CADI-R801	ARD-IBT-L'Oréal						Validated
Full Human Protein Glycosylation in yeast	CADI-R802	Open		high Interest				

“Disease-Centric” Repositioning Rational

Similar symptoms can have very different functional origins, while similar dysfunctions can produce different symptoms.

- Understanding and validating the mechanisms of a disease/disorder becomes the first objective. Finding the most adapted first in class solutions is a necessary consequence of the first objective.
- Life sciences mechanisms are complex, not complicated, and the digital “garbage in garbage out” is a growing reality.
- Do not forget that the “garbage in, garbage out” reality demonstrates that a wrong hypothesis, even if generated by top KOLs and/or treated by the best Digital and IT technologies, remain a wrong hypothesis!
- Novel therapies does not necessarily mean new drugs. Combo diagnostics and therapies are patentables

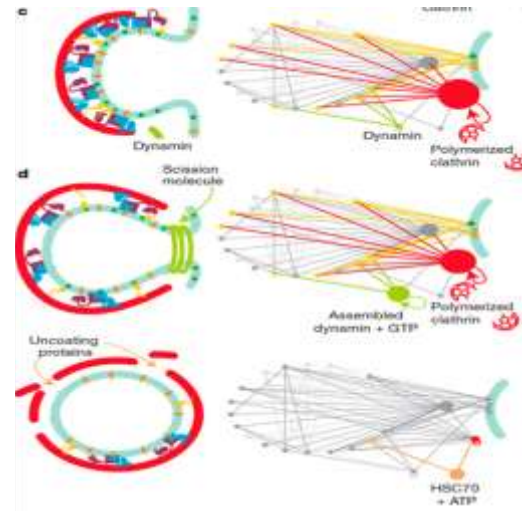
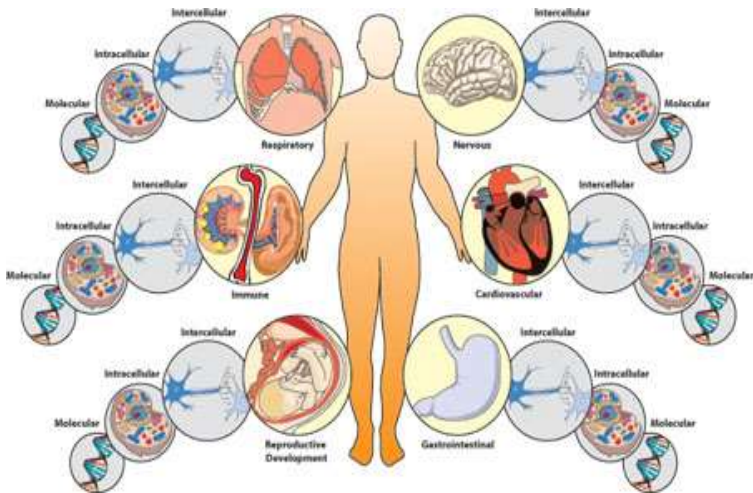
We invented in 2002 CADI™ Discovery, the world's first operational "Computer Augmented Deductive Intelligence" platform that natively combines Human Augmented intelligence and specialized algorithms.

To date, already generated robust heuristic models describing the complex mechanisms of the diseases that already led to first in class therapeutics, diagnostics and bio-production programs ready for development.

What leads to Therapeutic Success?

The success of a therapeutic approach largely arises from the coherent manipulation of a physiological system as a whole.

and not from that of a target in a molecular context.

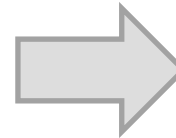


Therefore, any given medical problem should be approached from a "systems medicine" standpoint.

In this context, novel therapies can be combinations of drugs, nutriment, devices, e-health, etc...while targeted therapies belong to the "target in a molecular context" concept
Do not forget: Mechanisms of action or function of a target, drug, gene, etc.. ARE NOT the mechanisms of a complex disease / disorder

The Research & Development Answer

From: Evidence-Based Medicine To: Mechanisms-Based Medicine



- 1-DISEASE/DISORDER
- 2-MECHANISMS
- 3-BIOMARKERS
- 4-TARGETS
- 5-SOLUTIONS
- 6-VALIDATION

Understanding and validating the mechanisms of a disease/disorder becomes the first objective.
Finding the most adapted solutions is a necessary consequence of the first objective

5 R&D programs that led to combo-solutions



Microbiota & Autism therapeutic H2020 program started with 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 and therapeutic evaluation for metabolic disorders program self funded. UMANG program (Now implemented by Arbuza Regenerate Pvt Ltd) How does maternal nutrient restriction coupled with defective one-carbon metabolism alter the foetal development program, leading to enhanced predisposition to T2D in adolescence? Center 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. This therapy will also be applied to Gul war Syndrome



Therapeutic evaluation program self funded. Parkinson's disease and metabolic syndrome. The program led to a combinatorial therapeutic approach utilizing two molecules that had long been on the market, neither of which has any known toxicity or undesirable effects. Evaluation status: Discussion with confidential partners



Causal metabolic mechanisms of Alzheimer Disease (AD) model was produced by Bio-Modeling System in 2017-2018. The model in its current state is able to produce biomarkers that could probably predict or increase alertness for identifying AD at its very early stages of progression. Discover the 14 key components explained

BMSystems' Combo Therapeutics-Diagnostics-BioProduction CADI™ pipeline*

Internal Program Name	Indication	Pre-clinic	Phase I	Phase 2a	Phase 2b	Comp. Use	Phase 3
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COMBO-THERAPIES

CADI-T1011	Multi-resistance infectious diseases						Started
CADI-T1031	CFS/ME low-grade chronic inflammation		Ready				
CADI-T1032	Gulf War Syndrome	Ready					
CADI-T2011	Attenuation of the Core Symptoms of Autism		Ready				
CADI-T3021	Parkinson's Disease		Ready				
CADI-T4021	Attenuation of Developmental Consequences of Children Malnutrition		Ready				
CADI-T4031	Metabolic Syndrome		Ready				

Internal Program Name	Indication	Pre-clinic	Clinic
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COMBO-DIAGNOSTICS

CADI-D3041	Alzheimer's Disease Early Diagnostics		Ready
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Internal Program Name	Program Domains	Partners	CADI™ vers. 0	Ind. Valid.	Secret or Patent or Co-Patent/Publi.	First Proof of Concept (POC)
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CADI™-BIOPRODUCTION

CADI-B8011	Program Synthons (16 molecules study)		ARD-IBT-L'Oréal-Arkema-Solvay			Completed
CADI-B8021	Full Human Protein Glycosylation in yeast	Open		Ready		

* New internal classification

Thank you for your attention

Questions?



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