BMM 5787 COMPOSTOS BIOATIVOS E ESTRATEGIAS DE DESENVOLVIMENTO DE DROGAS

2ª e 4ª 17 de setembro à 7 de novembro

Horário 9-11

Sala Fava Neto

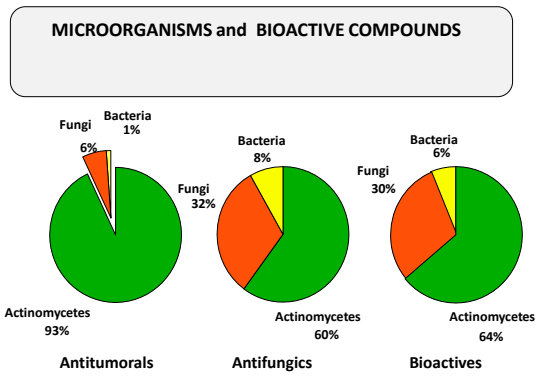
Professores Responsáveis: Gabriel Padilla e Márcio B. Dias

Data	Tema	Professor
2ª. 17/9	Compostos bioativos	Gabriel
4ª. 19/9	Antibióticos	Gabriel
2ª. 24/9	Biossíntese de antibióticos	Márcio
4ª. 26/9	Estratégias de desenho de farmácos	Márcio
2ª. 1/10	Moléculas de reserva	Gregório
4ª. 3/10	Biomoléculas de origem marinho	Paul Long
2ª. 8/10	Técnicas de screening	Carolina
4ª. 10/10	Interação plantas-microrganismos	Welington
2ª. 15/10	Compostos bioativos de origem marinha	Leticia
4ª. 17/10	Antifúngicos	Kelly
2ª. 22/10	Peptídeos	Ricardo
4ª. 24/10	Explorando nichos inéditos	Suiki
2ª. 29/10	Tratamento de câncer	Patrícia
4ª. 31/10	Reposicionamento de drogas	Lúcio
2ª. 5/11	Seminários *	Márcio-Gabriel
4ª. 7/11	Seminários* /Prova	Márcio-Gabriel

Todos os alunos tem a obrigação de preparar todos temas/artigos de referências que serão indicadas. Na hora será feito um sorteio para escolher o aluno que apresentará o artigo

Bioproducts Laboratory

Gabriel Padilla
Biomedical Sciences Institute
University of São Paulo



Natural products: molecules synthesized by an organism (uni/pluricellular) with biological activity in the producer and/or in a target cell. Bioactive products, compounds, natural products.

Bioactive compounds are defined as components of food that influence physiological or cellular activities in the animals or humans that consume them.

From: Molecular Nutrition and Diabetes, 2016

Bioactive compounds are phytochemicals found in foods that are capable of modulating metabolic processes and resulting in the promotion of better health.

Biotechnological applications:

Bioactive compounds are molecules with proven activities in various biological screenings and pharmacological models with a special emphasis on stereoeselective synthesis. R&D aim is to provide a valuable information source of bioactive compounds synthesized or isolated, which can be used for further development of pharmaceuticals by industry and academia.

NATURAL PRODUCTS

N.P's are chemical compounds or substance produced by a living organism—that are found in nature.

http://www.plantscience4u.com/2013/02/primary-and-secondary-metabolites.html#.VR99wvnGlk0

N.P's sometimes have pharmacological or biological activity that can be of therapeutic benefit in treating diseases

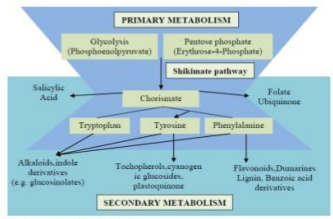
P. M. Dewick. Medicinal Natural Products, A Biosynthetic Approach. Second Edition (2002). John Wiley & Sons. England

4

NATURAL PRODUCTS

Within the field of O.C., the ***N.P's*** are usually restricted to mean purified organic compounds isolated from natural sources that are produced by the pathways:

- ✓ Primary metabolism
- ✓ Secondary metabolism



Edit by: Giovanny Rincon-Silva

O.C. : Organic Chemistry

P. M. Dewick. Medicinal Natural Products, A Biosynthetic Approach. Second Edition (2002). John Wiley & Sons. England

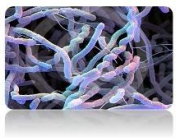
6

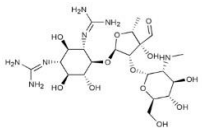
CLASSES & FUNCTIONS

N.P's are often divided into two major classes:

- **Primary metabolites:** have an intrinsic function that is essential to the survival of the organism that produces them.
- **Secondary metabolites:** have an extrinsic function that mainly affects other organisms.

Some secondary metabolites have useful medicinal properties.

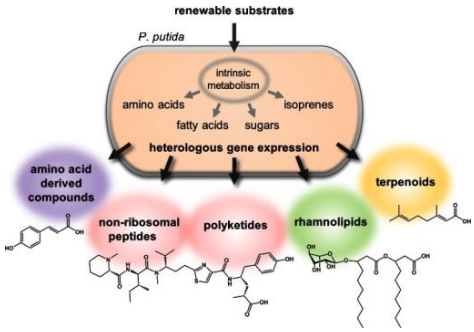


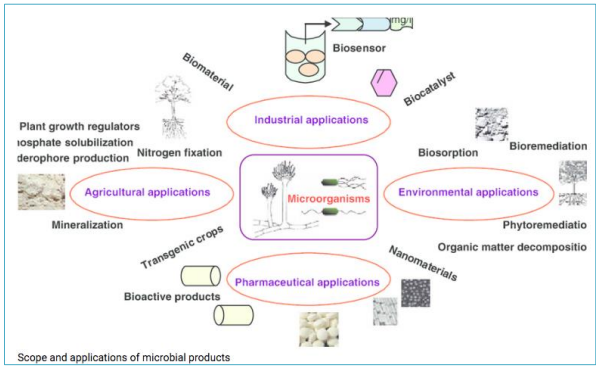


Streptomycin, an important antibiotic drug produced by Streptomyces bacteria

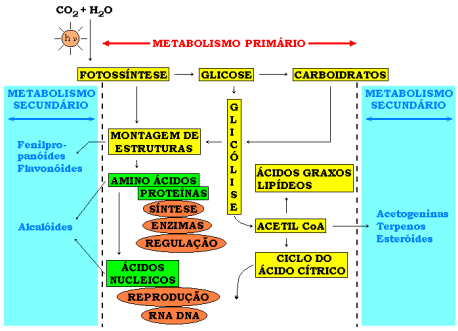
P. M. Dewick. Medicinal Natural Products, A Biosynthetic Approach. Second Edition (2002). John Wiley & Sons. England

7

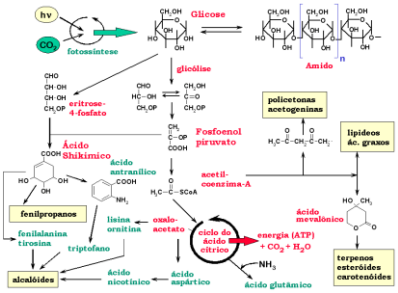




Scope and applications of microbial products

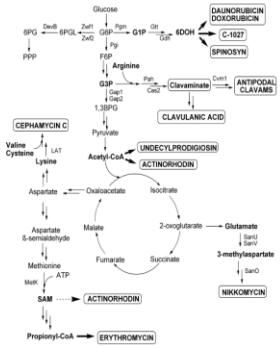


Metabolismo primário e secundário



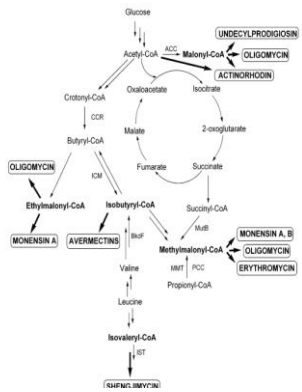
Metabolismo primário e secundário

Primary metabolism and production of antibiotics

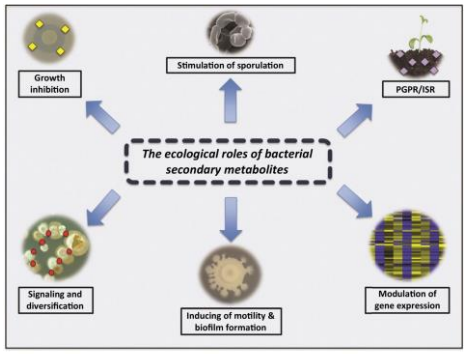


14

Fatty acids and secondary metabolites synthesis

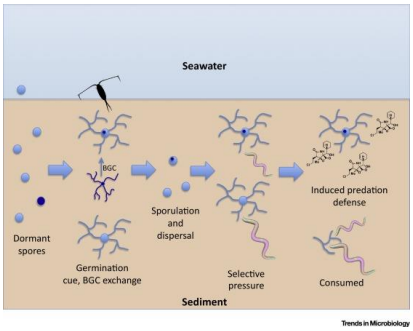


15

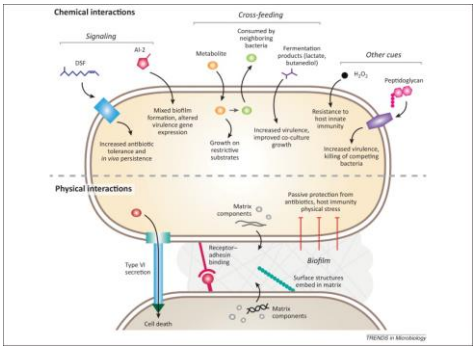


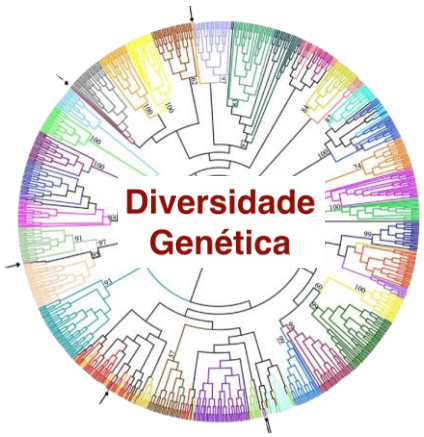
Ecological Roles of Bacterial Secondary Metabolites in Nature

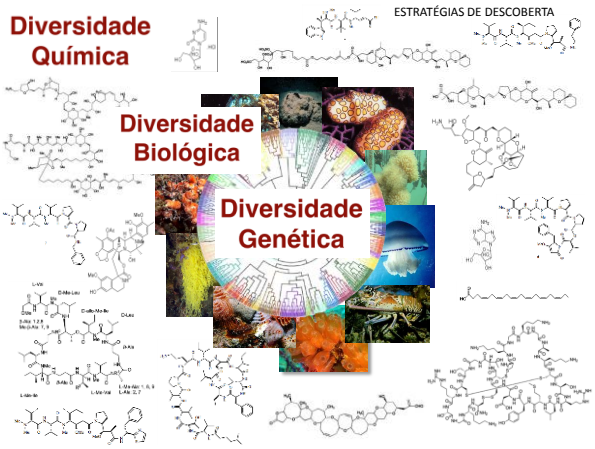
Ecological and evolutionary implications of seconday metabolism



BCGs biosynthetic gene clusters







Primary metabolites

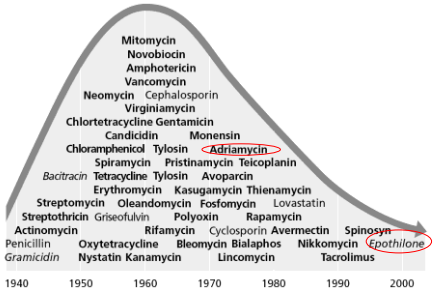
Proteins, peptides, enzymes, aminoacids, nucleic acids, vitamins, fatty acids, lipids

Secondary metabolites are conveniently classified based on their biosynthetic origin as terpenoids, polyketides, alkaloids, non-ribosomal peptides, cytochalasins

APPROACHES FOR SEARCHING NEW BIOACTIVE COMPOUNDS

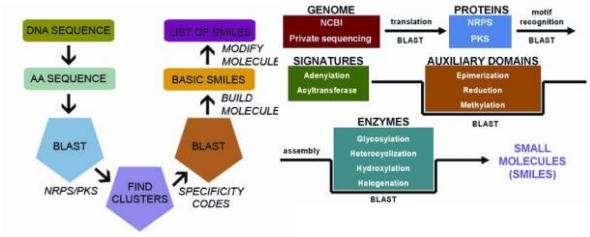
- COMBINATORIAL CHEMISTRY
  - Libraries of compounds from chemical synthesis
- NEW UNEXPLORED ECOLOGICAL NICHES
  - Marine organisms
  - Amazonas biodiversity
  - Endophytic organisms
  - Microbiome
- COMBINATORIAL BIOSYNTHESIS
  - Combination of genes from biosynthetic pathways of bioactiove compounds

Diminishing returns in finding natural products: Genetics to the rescue?

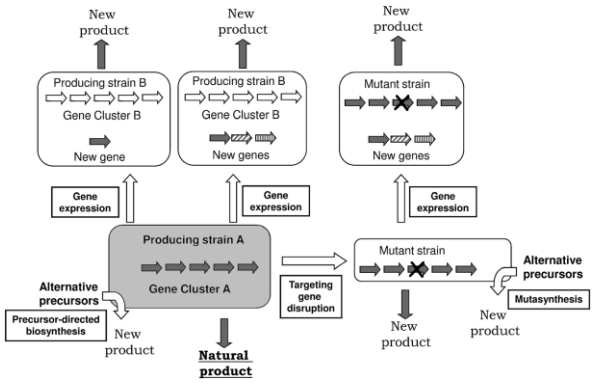


GENOME MINING

Previsão dos metabólitos produzidos pelo microorganismo a partir de suas seqüências genômicas, independentemente de seu cultivo



Stretagies used in combinatorial biosynthesis



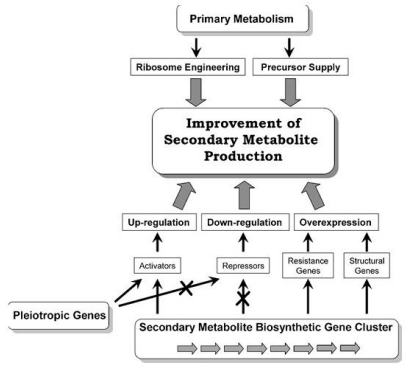
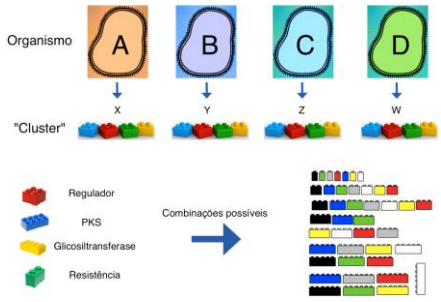


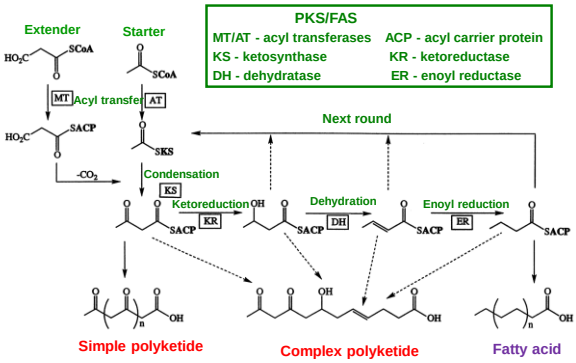
Fig. 1. Scheme representing the different approaches used for improvement of secondary metabolite production.

28

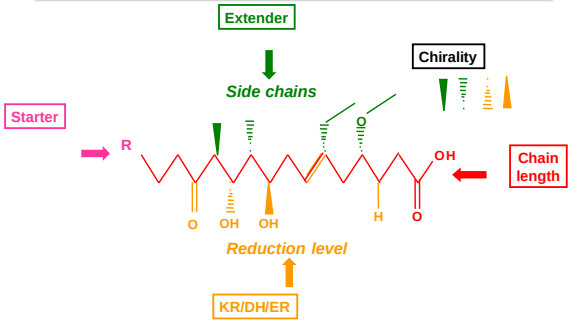
Combinatorial Biosynthesis



Fatty Acid and Polyketide Biosynthesis



Variables in Polyketides
('Combinatorial Biosynthesis')



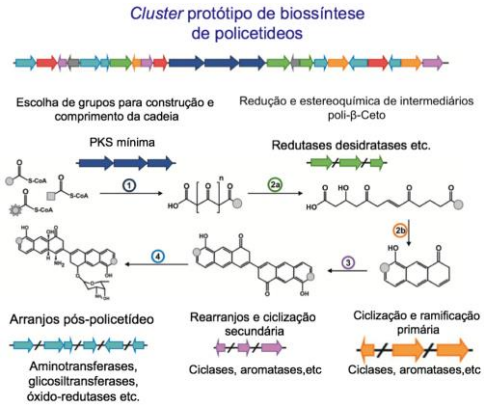
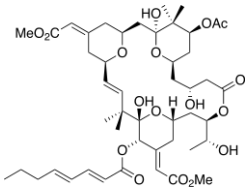
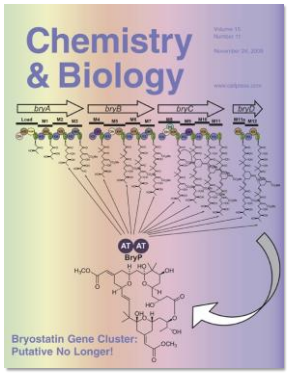


Figura 2. Ilustração esquemática das quatro etapas da biossíntese de policetídeos (Modificado de Cummings *et al*,2014) .

GENOME MINING

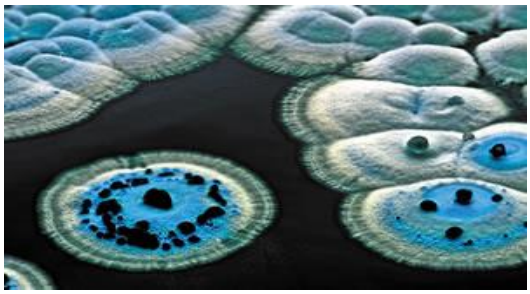


Briostatina 1
Pettit *et al.*, 1982

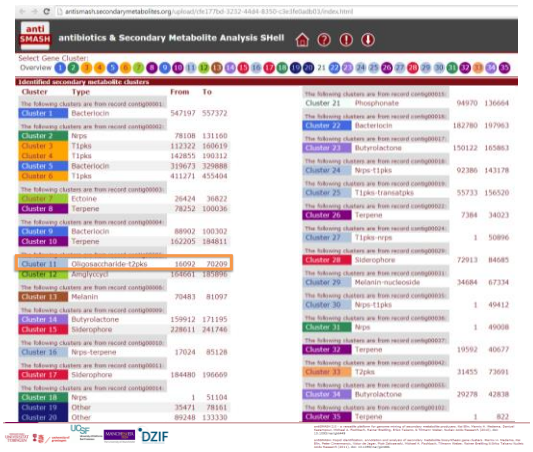


4 November, 2008
Volume 15, Issue 11, pp. 1139-1240

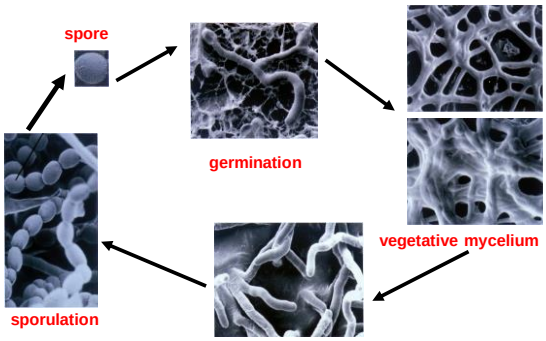
Streptomyces: A singular bacteria and a remarkable bio-factory



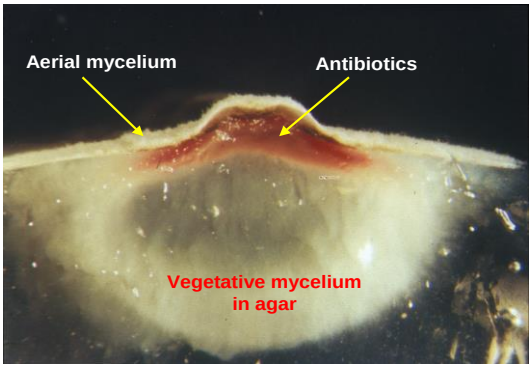
Generalised Morphology



Life cycle of *Streptomyces coelicolor*

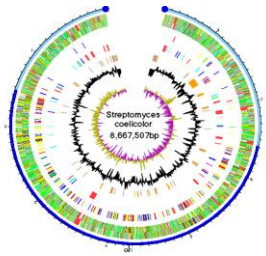


Cross-section through a *S. coelicolor* colony

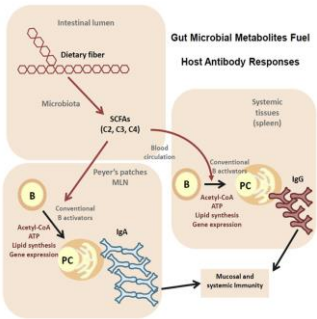


Escherichia coli K12

Genome
4 639 221
genes
4377
4290 proteins
87 RNAs



7825 Genes


Intestinal lumen
Dietary fiber
Microbiota
SCFAs
(C2, C3, C4)
Gut Microbial Metabolites Fuel
Host Antibody Responses
Systemic
tissues
(spleen)
Blood
circulation
Peyer's patches
MLN
B
Conventional
B activators
Acetyl-CoA
ATP
Lipid synthesis
Gene expression
PC
IgA
IgG
Mucosal and
systemic immunity