
Plan Overview

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Title: STUDY OF THE MODULATORY ACTION OF CROTOXIN IN THE GENE Slc11a1 S ALLELE EFFECTS ON THE EVOLUTION OF EXPERIMENTAL ULCERATIVE COLITIS.

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Project abstract:

Ulcerative colitis is considered an inflammatory disease characterized by a chronic lesion of the colon mucosa and associated with an increased risk of carcinogenesis. The pathogenesis of the disease involves environmental and genetic factors with active participation of phagocytic inflammatory cells, particularly activated macrophages. Genetic studies in humans indicate the association of variants of the gene encoding the Slc11a1 (or Nramp1) ion transport protein with susceptibility to this disease. This protein has pleiotropic effects on macrophages, influencing its inflammatory, tumoricidal and antimicrobial activities. The most appropriate experimental study model for ulcerative colitis has been done through the ingestion of sodium dextran sulfate in susceptible animals. The mice genetically selected for high (AIRmax) or low acute inflammatory response (AIRmin) to subcutaneous Biogel showed different behaviors for DSS ingestion, in addition to differentiated fixation of the R and S alleles to the Slc11a1 locus, evaluated by genotyping and resistance phenotypes. or susceptibility to infection by Salmonella enterica serotype Typhimurium. Homozygous sub-strains for the Slc11a1 R and S alleles were then obtained for both AIRmax and AIRmin strains and demonstrated that gene interactions between these alleles and the genes selected for AIR result in the modulation of resistance or susceptibility to infection and inflammatory response phenotypes. We hypothesized that Crotoxin could modulate the effects of the sensitivity allele (s) of the Slc11a1 gene in UC, since it has important anti-inflammatory effects. Thus, we will study the direct relationship between the response to DSS and the presence of R and S alleles for the Slc11a1 locus in animals selected for AIR with these alleles fixed in homozygosity, AIRmaxRR, AIRmaxSS, AIRminRR and AIRminSS treated or not with Crotoxin. This study will take place through the evaluation of parameters involved in UC, such as clinical, immunological and molecular aspects, aiming at the identification of therapeutic targets for the control of this pathology.

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STUDY OF THE MODULATORY ACTION OF CROTOXIN IN THE GENE *Slc11a1* S ALLELE EFFECTS ON THE EVOLUTION OF EXPERIMENTAL ULCERATIVE COLITIS.

Data Collection

What data will you collect or create?

O objetivo deste trabalho é o de estudar a influência do gene *Slc11a1* no fenótipo de resistência ou suscetibilidade à colite ulcerativa induzida por DSS, assim como os mecanismos envolvidos na resposta inflamatória durante a evolução do processo de lesão tecidual na vigência de tratamento com Crotoxina, forneceremos dados como o índice de atividade da doença, os efeitos de uma possível modulação da crotoxina sobre o gene *Slc11a1*, além de avaliar o perfil de citocinas expressas no intestino dos animais tratados ou não com DSS e CTX. Pretendemos realizar a análise da microbiota intestinal desses animais e verificar a importância das bactérias durante o processo inflamatório. Avaliaremos também as junções intracelulares da mucosa intestinal, afim de verificar possíveis alterações decorrentes da doença.

How will the data be collected or created?

Question not answered.

Documentation and Metadata

What documentation and metadata will accompany the data?

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Ethics and Legal Compliance

How will you manage any ethical issues?

O projeto já foi aprovado pelo comitê de ética do Instituto Butantan, protocolado sob o CEUA nº 4195190820.

How will you manage copyright and Intellectual Property Rights (IPR) issues?

O projeto terá direitos autorais em relação aos dados gerados, com cópias arquivadas no próprio laboratório.

Storage and Backup

How will the data be stored and backed up during the research?

Os dados serão armazenados de forma segura no próprio laboratório e em arquivos compartilhados entre os pesquisadores responsáveis pelo projeto.

How will you manage access and security?

Até que haja a publicação dos dados, todos os resultados ficarão em arquivos protegidos por senhas institucionais e pessoais.

Selection and Preservation**Which data are of long-term value and should be retained, shared, and/or preserved?**

Todos os dados obtidos com esse projeto ficarão disponíveis para consulta, através de publicações em revistas científicas e através da publicação da tese de doutorado.

What is the long-term preservation plan for the dataset?**Data Sharing****How will you share the data?**

Para o compartilhamento dos dados, publicaremos os resultados em revistas científicas e em bancos de dados específicos.

Are any restrictions on data sharing required?

Não há restrições para o compartilhamento dos dados.

Responsibilities and Resources**Who will be responsible for data management?**

Os pesquisadores envolvidos no projeto serão os responsáveis pelo gerenciamento dos dados.

What resources will you require to deliver your plan?

Serão necessários softwares para análise dos dados, e conhecimento prévio a cerca das técnicas que serão empregadas para o desenvolvimento do projeto.