europass

Margherita Degasperi

di nascita: 12/11/1991

Nazionalità: Italiana

CONTATTI

ESPERIENZA LAVORATIVA

01/09/2023 – ATTUALE Basovizza, Italia

Tecnologo in genomica Area science park- Laboratory of Genomic and Epigenomic (LAGE)

Le attività di ricerca svolte si inseriscono all'interno del macroambito del next generation sequencing (NGS) con un'attenzione particolare a:

- implementazione di protocolli per la preparazione di librerie di single cells
- implementazione di protocolli di ingegneria genetica in colture cellulari tramite la tecnologia Crispr-Cas9 per sequenziamento long reads con piattaforme Oxford Nanopore;
- implementazione di protocolli di preparazione di campioni biologici e per Spatial Transcriptomics (ST) e successiva preparazione di librerie con tecnologie di sequenziamento di terza generazione;
- implementazione di protocolli di preparazione di campioni biologici e librerie per analisi di “Proteogenomics”;

15/07/2021 – 31/08/2023 Basovizza, Italia

Assegnista di ricerca Area science park- Laboratory of Genomic and Epigenomic (LAGE)

Le attività di ricerca svolte si inseriscono nell’ambito del Progetto PON “BIO Open Lab (BOL) - Rafforzamento del capitale umano” – CUP J72F20000940007 e sono incentrate sulla creazione di una facility di Next Generation Sequencing. Il tema della ricerca è l’implementazione di nuovi protocolli di sequenza derivanti dalle tecnologie di sequenziamento a singola molecola su piattaforma Oxford Nanopore. Rispetto al sequenziamento NGS, queste tecnologie non necessitano di passaggi di amplificazione (PCR), permettendo potenzialmente analisi delle molecole native e non tramite passaggi indiretti. In particolare, il focus dell’assegno riguarda lo sviluppo e l’ottimizzazione di protocolli per lo studio di varianti strutturali o di splicing dell’RNA, per lo studio di modifiche dirette nel DNA ed RNA nativo (epigenomica) e per la preparazione e il sequenziamento di molecole di DNA Ultra long (>80 kb). La piattaforma di sequenziamento utilizzata in questo contesto è il PromethION, per la quale continuo a seguire corsi di aggiornamento.

30/09/2020 – 14/07/2021 Basovizza, Italia

Assegnista di ricerca Area science park- Laboratory of Genomic and Epigenomic (LAGE)

Le attività svolte riguardano protocolli di next- generation sequencing (NGS) tra cui: exome sequencing, RNA-
seq, sequenziamento di DNA metilato e sequenziamento a singola molecola. In questo ambito, mi occupo sia della fase di preparazione delle librerie di DNA/RNA sia della gestione diretta del sequenziatore. Le maggiori piattaforme di sequenziamento con cui mi interfaccio sono di tipo Illumina
(MiSeq, NovaSeq, HiScan e iScan) e Oxfordnanopore (MinION e Promet hION) per le quali ho seguito dei training specifici, diventando autonoma nel loro utilizzo.

Impresa o settore Attività professionali, scientifiche e tecniche

30/09/2019 – 29/09/2020

Assegnista di ricerca Università degli Studi di Trieste

Settore disciplinare: BIO/13 - BIOLOGIA APPLICATA, titolo del progetto: "Selezione e caratterizzazione di anticorpi monoclonali diretti contro il recettore del folato".
L'attività del progetto era incentrata sulla ricerca di anticorpi monoclonali specifici contro il recettore folato tramite la tecnica del phage display. Le principali competenze richieste sono state:

- isolamento di anticorpi ricambianti mediante Phage display

- espressione e purificazione come scFVS-FC degli anticorpi precedentemente isolati
- caratterizzazione in vitro di specificità e selettività
- valutazione del legame sulla superficie cellulare e del loro possibile uso terapeutico su diverse linee cellulari di tumore ovarico

30/09/2019 – 19/12/2019 Trieste, Italia

Tutorato Biochimica II Università degli Studi di Trieste

Tutorato teorico e pratico di Biochimica II (metabolismo cellulare e integrazione delle vie metaboliche) per il corso di laurea in science e tecnologie biologiche- Dipartimento di scienze della vita presso l'università di Trieste. 50 ore totali

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ISTRUZIONE E FORMAZIONE

31/10/2015 – 30/10/2018

Dottorato in Biomedicina Molecolare Università degli Studi di Trieste

30/09/2013 – 24/10/2015

Laurea specialistica in Genomica Funzionale (LM-6) - 110/110 cum laude Università degli Studi di Trieste

30/09/2010 – 30/09/2013

Laurea triennale in Biologia Molecolare (L13)- 110/110 cum laude Università degli Studi di Padova

COMPETENZE LINGUISTICHE

LINGUA MADRE: italiano

Altre lingue:

inglese

Ascolto	Lettura	Produzione orale	Interazione orale	Scrittura
B1	B1	B1	B1	B1

francese

Ascolto	Lettura	Produzione orale	Interazione orale	Scrittura
A1	A1	A1	A1	A1

Livelli: A1 e A2: Livello elementare B1 e B2: Livello intermedio C1 e C2: Livello avanzato

COMPETENZE DIGITALI

Microsoft Office | Microsoft Word | Microsoft Excel | Microsoft Powerpoint | Outlook | Google Drive

ULTERIORI INFORMAZIONI

Abilità e competenze

Competenze in Next-Generation Sequencing

Durante questi anni di assegni di ricerca presso il laboratorio LAGE di Area Science Park mi sto occupando di next-generation sequencing (NGS).
Inizialmente mi sono interfacciata soprattutto con le tecnologie e i protocolli di library prep Illumina. In questo ambito ho sviluppato buone competenze tecniche nel sequenziamento massivo in parallelo e nella gestione autonoma degli strumenti di sequenziamento Illumina (MiSeq, NovaSeq, HiScan e iScan). In particolare, sono stata formata su Whole-exome/whole-genome sequencing, sequenziamento del DNA metilato, sequenziamento metagenomico, RNA-seq/ mRNA-seq e miRNA seq.
Successivamente mi sono concentrata sul sequenziamento a singola molecola reso possibile dall'utilizzo delle piattaforme di sequenziamento Oxford Nanopore. In questo contesto mi sono soprattutto focalizzata sul sequenziamento di DNA e RNA nativo e sull'ottimizzazione di protocolli per lo studio delle varianti strutturali di queste molecole (epigenetica). In parallelo mi sono occupata di protocolli di estrazione di gDNA ad alto peso molecolare a partire da pelle cellulari e del sequenziamento di molecole di gDNA Ultra-long (>80kb) che risultano particolarmente promettenti nel caso di studi di de novo assembly. Le piattaforme Oxford Nanopore con cui ho maggiore confidenza sono MinION e PromethION.
Sia per l'utilizzo delle piattaforme Illumina che Oxford Nanopore ho seguito training specifici di formazione che mi hanno consentito di sviluppare un'autonomia di lavoro

Competenze di Biologia Molecolare

Ho buone capacità nel campo della biologia molecolare e del Phage display.
Per quanto riguarda la biologia molecolare ho una solida pratica in: qPCR, estrazione di acidi nucleici, SDS-PAGE, purificazione di DNA da gel di agarosio, protocolli di digestione-ligazione-clonaggio, trasformazione di cellule chimico competenti ed per elettroporazione e infine Western blot. Per quanto riguarda il campo del Phage display, ho sviluppato autonomia: nella selezione/biopanning/eluizione (su supposto solido o su biglie), phage ELISA, produzione di anticorpi monoclonali in cellule eucariotiche (CHO) e purificazione proteica su resina (resine con proteina A, Ni-NTA).

Competenze in Microbiologia

Ho un background molto solido in microbiologia.
In particolare ho le competenze per maneggiare microorganismi di biosafety level 2 e ho buone conoscenze nei saggi di MIC e MBC (anche in diversi medium come Mueller Hinton, siero, lavaggio broncoalveolare) per testare l'attività antimicrobica di composti contro funghi e batteri.
Ho sviluppato buona padronanza di saggi anti-biofilm batterico e fungine, sia in termini di inibizione della formazione di nuovo biofilm sia di eradicazione di biofilm preformati valutati sia tramite saggi MTT che Cristalvioletto.
Ho una buona capacità nel mantenimento di colture cellule eucariotiche sia in sospensione che in adesione e nella valutazione della citotossicità di molecole VS queste tramite saggio MTT.

Competenze in Bioinformatica

Conoscenza di programmi bioinformatici per l'analisi genetica dei dati, quali EPI2ME labs, GenomeStudio e IGV
Utilizzo di banche dati quali GISAID e ENA

Pubblicazioni

Mitochondrial Metabolism and EV Cargo of Endothelial Cells Is Affected in Presence of EVs Derived from MSCs on Which HIF Is Activated

2023

Abstract: Small extracellular vesicles (sEVs) derived from mesenchymal stem cells (MSCs) have attracted growing interest as a possible novel therapeutic agent for the management of different cardiovascular diseases (CVDs). Hypoxia significantly enhances the secretion of angiogenic mediators from MSCs as well as sEVs. The iron-chelating deferoxamine mesylate (DFO) is a stabilizer of hypoxia- inducible factor 1 and consequently used as a substitute for environmental hypoxia. The improved regenerative potential of DFO-treated MSCs has been attributed to the increased release of angiogenic factors, but whether this effect is also mediated by the secreted sEVs has not yet been investigated. In this study, we treated adipose-derived stem cells (ASCs) with a nontoxic dose of DFO to harvest sEVs (DFO-sEVs). Human umbilical vein endothelial cells (HUVECs) treated with DFO-sEVs underwent mRNA sequencing and miRNA profiling of sEV cargo (HUVEC-sEVs). The transcriptomes revealed the upregulation of mitochondrial genes linked to oxidative phosphorylation. Functional enrichment analysis on miRNAs of HUVEC-sEVs showed a connection with the signaling pathways of cell proliferation and angiogenesis. In conclusion, mesenchymal cells treated with DFO release sEVs that induce in the recipient endothelial cells molecular pathways and biological processes strongly linked to proliferation and angiogenesis.

An Apple a Day Keeps the Doctor Away: Potential Role of miRNA 146 on Macrophages Treated with Exosomes Derived from Apples

2022

Abstract:
The constant dialogue between the plant world and the animal world (including man among them) has been known since the time of Adam and Eve, where an apple was the origin of the evils of the world. Apart from Snow White—who might have something to object to when it comes to the use of apples—fruits, plants, and natural extracts have been known for millennia as remedies for human health-related ailments. In the light of such evidence, the aim of the present work was to investigate from a biological point of view the potential role of apple exosomes in inflammatory processes on human cells. To this end we isolated and characterized apple exosomes and treated human cells such as macrophages and NCTC L929 as cancer cells in order to evaluate the tumorigenic and anti-inflammatory effect of apple exomes. Microscopic and molecular biology analyses were conducted to characterize exosomes and to assess cell proliferation, death, and miRNA line, as well as gene expression and the uptake of exosomes by cells. The results confirm the absolute biological safety of exosomes and their anti-inflammatory effect, mediated mainly by miRNA146 production by M2 macrophages

Elastase-Activated Antimicrobial Peptide for a Safer Pulmonary Treatment of Cystic Fibrosis Infections

2022

Abstract:
As bioactive small proteins with antimicrobial and immunomodulatory activities that are naturally produced by all living organisms, antimicrobial peptides (AMPs) have a marked potential as next-generation antibiotics. However, their development as antibacterial agents is limited by low stability and cytotoxicity. D-BMAP18, a membrane-permeabilizing antimicrobial peptide composed of D-amino acids, has shown good antibacterial and anti-inflammatory activities but also a non-negligible cytotoxicity against eukaryotic cell lines. In this study, a prodrug has been developed that extends the peptide with a negatively charged, inactivating sequence containing the cleavage site for neutrophil elastase (NE). The ultimate goal was to allow the activation of D-BMAP18 by endogenous elastase only at the site of infection/inflammation, enabling a slow and targeted release of the pharmacologically active peptide. In vitro activation of Pro-D-BMAP18 was confirmed using purified NE. Its antimicrobial and cytotoxic activities were tested in the presence and absence of elastase and compared to those of the parental form. The prodrug had minimal activity in the absence of elastase, while its proteolysis product retained an appreciable antimicrobial activity but lower cytotoxicity. Moreover, Pro-D-BMAP18 was found to be correctly converted to D-BMAP18 in the presence of CF sputum as a model of the lung environment and showed good antimicrobial activity under these conditions.

The anti-pseudomonal peptide D-BMAP18 is active in Cystic Fibrosis sputum and displays anti-anflammatory in vitro activity.

2020

Abstract:
Most Cystic Fibrosis (CF) patients succumb to airway inflammation and pulmonary infections due to *Pseud omonas aeruginosa*. *D*-BMAP18, a membrane-permeabilizing antimicrobial peptide composed of D-amino acids, was evaluated as a possible antibacterial aimed to address this issue. The antipseudomonal activity of *D*-BMAP18 was tested in a pathophysiological context. The peptide displayed activity against CF isolates of *Pseudomonas aeruginosa* in the presence of CF sputum when combined with sodium chloride and DNase I. In combination with DNase I, *D*-BMAP18 discouraged the deposition of new biofilm and eradicated preformed biofilms of some *P. aeruginosa* strains. In addition, *D*-BMAP18 down regulated the production of TNF-α, IL1-β, and TGF-β in LPS-stimulated or IFN-γ macrophages derived from THP-1 cells indicating an anti-inflammatory activity. The biocompatibility of *D*-BMAP18 was assessed using four different cell lines, showing that residual cell-specific cytotoxicity at bactericidal concentrations could be abolished by the presence of CF sputum. Overall, this study suggests that *D*-BMAP18 may be an interesting molecule as a starting point to develop a novel therapeutic agent to simultaneously contrast lung infections and inflammation in CF patients.

Search for shorter portions of the proline-rich antimicrobial peptide fragment Bac5(1-25) retaining antimicrobial activity by blocking protein synthesis

2019

Abstract:
The spread of antibiotic-resistant pathogens has boosted the search for new antimicrobial drugs. Proline-rich antimicrobial peptides are promising lead compounds for the development of next-generation antibiotics, given their very low cytotoxicity and their good antimicrobial activity targeting the bacterial ri-bosome. Bac5(1–25) is an N-terminal fragment of the bovine proline-rich antimicrobial peptide Bac5, whose mode of action has been recently described. In this work we tested a number of Bac5(1–25) fragments, and we characterized their antimicro-
bial activity against Escherichia coli, Acinetobacter baumannii, Klebsiella pneumoniae, Staphylococcus aureus, Salmonella enteri- ca, and Pseudomonas aeruginosa. We evaluated their cytotoxicity toward human cells and their efficacy in inhibiting bacterial protein synthesis. This allowed us to identify some shorter fragments of Bac5(1–25) with a good balance between anti- bacterial efficacy, protein synthesis inhibition, and ease/cost-effectiveness of synthesis, suitable as lead compounds to develop new antibacterials.

D-BMAP18 antimicrobial peptide is active in vitro, resists to pulmonary proteases but loses its activity in a murine model of Pseudomonas aeruginosa lung infection.

2017

Abstract:
The spread of antibiotic resistant-pathogens is driving the search for new antimicrobial compounds. Pulmonary infections experienced by cystic fibrosis (CF) patients are a dramatic example of this health-care emergency. Antimicrobial peptides could answer the need for new antibiotics but translating them from basic research to the clinic is a challenge. We have previously evaluated the potential of the small membranolytic peptide BMAP-18 to treat CF-related infections, discovering that while this molecule had a good activity *in vitro* it was not active *in vivo* because of its rapid degradation by pulmonary proteases. In this study, we synthesized and tested the proteases-resistant all-*d* enantiomer. In spite of a good antimicrobial activity against *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia* clinical isolates and of a tolerable cytotoxicity *in vitro, D*-BMAP18 was ineffective to treat *P. aeruginosa* pulmonary infection in mice, in comparison to tobramycin. We observed that different factors other than peptide degradation hampered its efficacy for pulmonary application. These results indicate that *D*-BMAP18 needs further optimization before being suitable for clinical application and this approach may represent a guide for optimization of other anti-infective peptides eligible for the treatment of pulmonary infections.

In vitro and in vivo evaluation of BMAP-derived peptides for the treatment of cystic fibrosis-related pulmonary infections.

2016

Abstract:
Patients with cystic fibrosis require pharmacological treatment against chronic lung infections. The alpha-helical antimicrobial peptides BMAP-27 and BMAP-28 have shown to be highly active in vitro against planktonic and sessile forms of multidrug-resistant *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *St enotrophomonas maltophilia* cystic fibrosis strains. To develop small antibacterial peptides for therapeutic use, we tested shortened/modified BMAP fragments, and selected the one with the highest in vitro antibacterial activity and lowest in vivo acute pulmonary toxicity. All the new peptides have shown to roughly maintain their antibacterial activity in vitro. The 1–18 N-terminal fragment of BMAP-27, showing MIC90 of 16 µg/ml against *P. aeruginosa* isolates and strain-dependent anti-biofilm effects, showed the lowest pulmonary toxicity in mice. However, when tested in a murine model of acute lung infection by *P. aeruginosa*, BMAP-27(1–18) did not show any curative effect. If exposed to murine broncho-alveolar lavage fluid BMAP-27(1–18) was degraded within 10 min, suggesting it is not stable in pulmonary environment, probably due to murine proteases. Our results indicate that shortened BMAP peptides could represent a starting point for antibacterial drugs, but they also indicate that they need a further optimization for effective in vivo use.

Conferenze e seminari

31/03/2023 – 31/03/2023 Milano

Single-molecule Sequencing Technologies & Applications L'evento è stato organizzato dallo Human technopole con lo scopo di fare un punto sullo stato dell'arte del sequenziamento a singola molecola.
La giornata è stata divisa in due macroambiti. La prima parte riguardava il sequenziamento diretto di RNA sia dal punto di vista di preparazione della libreria che di analisi dati (identificazione di varianti strutturali, varianti di splicing, modificazioni su molecola nativa).
La seconda parte era focalizzata sul sequenziamento del DNA e sull'importanza dell'ottenimento si sequenze ultra lunghe per il de novo assembly

29/03/2023 – 29/03/2023 Milano

Experience the Power of Spatial Biology Organizzato da Nanostring e Diatech, il congresso aveva lo scopo principale di mostrare gli avanzamenti tecnologici fatti nell'ambito della spatial transcriptomic (ST) e di presentare due strumentazioni di recente sviluppo.
Focus della giornata è stato osservare il funzionamento di due strumenti dedicati alla ST (il Geomx e il Cosmx) e iniziare una formazione dell'analisi dati con software proprietari

18/05/2022 – 20/05/2022 London- UK

London Calling 2022 London Calling is a conference dedicated to scientific research using nanopore DNA/RNA sequencing

18/05/2021 – 20/05/2021 London Calling is a conference dedicated to scientific research using nanopore DNA/RNA sequencing

London Calling 2021 London Calling is a conference dedicated to scientific research using nanopore DNA/RNA sequencing

26/02/2019 – 28/02/2019 Paris- France

13° European CF Young Investigators Meeting (EYIM) Poster and Oral presentation: "Characterization and optimization of D-BMAP18 for the *in vivo* treatment of CF pulmonary infections."

Abstract:

D-BMAP18 is an all-D and truncated form of the native bovine α-helical antimicrobial peptide BMAP27, investigated for its potential in treating cystic fibrosis (CF) pulmonary infections. D-BMAP18 shows high *in vitro* antimicrobial activity against multidrug-resistant CF-strains of *Pseudomonas aeruginosa* (*P.a.)* and it is stable in pulmonary environment [1,2]. At sub-inhibitory concentrations, D-BMAP18 inhibits *P.a.* biofilm formation and has good eradication activity against preformed biofilm. When evaluated in CF-sputum, mimicking the therapeutic environment, the peptide maintains its antibacterial activity. Moreover, its anti-inflammatory activity against the stimulated THP1 cells was proved. However, D-BMAP18 intratracheally administrated in murine lungs had a non-negligible toxicity [3] limiting its *in vivo* use as antibacterial. To overcome this side effect, we synthesized the pro-drug Pro-D-BMAP18, adding a negatively charged pro-sequence to the peptide, making it inactive and enzimatically activable only at the site of infection/ inflammation. We confirmed that Pro-D-BMAP18 lost most of its antimicrobial activity and that the active D-BMAP18 was proteolitically released *in vitro* by elastase secreted from neutrophil cell line. The activated Pro-D-BMAP18 regained the parental activity against planktonic and sessile forms of *P.a* and additionally, has a reduce cytotoxicity. Testing the peptide activation in CF-sputum, Pro-D-BMAP18 recovered its antimicrobial activity against *P.a*. and *Candida albicans*. This suggest that the release of D-BMAP18 from the pro-drug could correctly occur also in the lungs of patients thank to the endogenous elastase and that CF-sputum did not suppress peptide activity. Only further studies in a murine model of pulmonary *P.a.* pul monary infection, will establish the therapeutic potential of this antimicrobial peptide toward CF infections.

[1] Benincasa et al. (2003). Peptides 24: 1723-1731
[2] Mardirossian et al. (2016). Amino acids 48(9):2253-2260
[3] Mardirossian et al. (2017). Frontiers in Chemistry

01/09/2018 – 03/09/2018 Edinburgh- UK

8° International Meeting on Antimicrobial Peptide (IMAP 2018) Oral presentation: "Characterization and optimization of D-BMAP18 for the *in vivo* treatment of CF pulmonary infections"

Abstract:
D-BMAP18 is an all-D and truncated form of the native bovine α-helical antimicrobial peptide BMAP27, that was investigated for its potential in treatment of cystic fibrosis (CF) pulmonary infections. D-BMAP18 shows high *in vitro* antimicrobial activity against multidrug-resistant CF-strains of *Pseudomonas aeruginosa* (*P.a.)* and it is stable in pulmonary environment [1,2]. At sub-inhibitory concentrations, D-BMAP18 inhibits *P.a.* biofilm formation and has good eradication activity against preformed biofilm. Moreover, the peptide maintains its antibacterial and antifungal activities also in CF-sputum. However, D-BMAP18 intratracheally administrated in murine lungs had non-negligible toxicity [3] limiting its *in vivo* use as antibacterial. To overcome this side effect, we synthesized the pro-drug Pro-D-BMAP18, adding a negatively charged pro-sequence to the peptide, making it inactive and enzimatically activable only at the site of infection/inflammation. We confirmed that Pro-D-BMAP18 lost most of its antimicrobial activity and that the active D-BMAP18 was proteolitically released *in vitro* by elastase secreted from neutrophil cell line. The activated Pro-D-BMAP18 regained the parental activity against planktonic and sessile forms of *P. a*. Testing the peptide activation in CF-sputum, Pro-D-BMAP18 recovered its antimicrobial activity against *P.a*. and *Candida albicans*. This suggest that the release of D-BMAP18 from the pro-drug could correctly occur also in the lungs of patients and that CF-sputum did not suppress peptide activity. *In vivo* o ngoing experiments on D-BMAP18 toxicity and activity in *Galleria mellonella* larvae, and studies in a murine model of pulmonary *P.a.* infection, will establish the therapeutic potential of this antimicrobial peptide toward CF pulmonary infections.

[1] Benincasa et al. (2003). Peptides 24: 1723-1731
[2] Mardirossian et al. (2016). Amino acids 48(9):2253-2260
[3] Mardirossian et al. (2017). Frontiers in Chemistry

04/07/2018 – 05/07/2018 Naples- Italy

2° National Congress of the Italian Antimicrobial Peptide Society Oral presentation: "*In vitro* and *in vivo* evaluation of D-BMAP18 peptide for the treatment of pulmonary infections in cystic fibrosis"

Abstract:
Patients with cystic fibrosis require pharmacological treatment against chronic lung infections due to antibiotic resistant pathogens. Antimicrobial peptides are among the leading compound for developing new drugs because of the broad spectrum of activity and the slow rate in acquire resistance. In order to obtain a peptide stable in the pulmonary environment we truncated and modified the natural antimicrobial peptide BMAP27, obtaining the all-D peptide *D*-BMAP18 [1]. It is an α-helical peptide which has a MIC_{90}= 16 μg/ml against *Pseudomonas aeruginosa* CF-isolates [2] and has a good activity against their biofilm. We tested with success the bactericidal activity of *D*-BMAP18 toward *P. aeruginosa* in CF- sputum by co-treatments with DNase and NaCl. We also tested its *in vitro* and *in vivo*toxicity observing a non-negligible toxicity when it was intratracheally administrated to mice [3], a side effect that may be linked to this route of administration. Preliminary test on a systemic infection model in *Galleria mellonella* (wax moth) are in progress to verify this hypothesis. In order to improve its efficacy and to minimize undesired side effects, we are also trying new routes of administration in mice and the design of a modified *in situ* a ctivable D-BMAP18 prodrug. The final aim is to obtain a safe drug for the treatment of pulmonary infections in cystic fibrosis.

[1] Pompilio et al. (2011). Peptides 32: 1807-1814
[2] Mardirossian et al. (2016). Amino acids 48(9):2253-2260
[3] Mardirossian et al. (2017). Frontiers in Chemistry

06/07/2018 – 08/07/2018 Naples- Italy

16° Naples workshop on Bioactive Peptides Poster presentation: "*In vitro* and *in vivo* evaluation of D-BMAP18 peptide for the treatment of pulmonary infections in cystic fibrosis"

27/08/2017 – 29/08/2017 Trieste

2° PhD students' conference Oral presentation: "Optimization of BMAP18 peptides for the treatment of pulmonary infections"

Abstract:
Patients with pulmonary infection, including cystic fibrosis (CF) require pharmacological treatment. The therapy with common antibiotic caused the development of multidrug-resistant bacteria (MDR) and, in order to face them, new molecules are required [1]. In this scenery an emerging role is the one of the antimicrobial peptides (AMPs) [2] which are part of the eukaryotic immune-system and are characterized by a slow rate of acquired resistance. BMAP-28 and BMAP-27, two AMPs belonging to the cathelicidin family, have excellent *in vitro* antimicrobial activity, in some cases higher than that of the antibiotic tobramycin against planktonic and sessile forms of MDR *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia* CF strains, [3]. Despite their activity these molecule showed signs of toxicity when intratracheally administered in the lungs of mice. Different shortened BMAP fragments were tested. Among them two peptides have been selected: the 18-mer fragment L-BMAP18 and its all-D enantiomer D-BMAP18. The first had been selected for its higher activity and lowest toxicity [4] but unfortunately it is rapidly degraded in the murine bronchoalveolar lavage fluid (BALF) [5] and therefore it does not possess a significant protective activity. The latter (D-BMAP-18) has shown to be active as antimicrobial and also to be stable in BALF but, on the other hand, it had a higher *in vitro* and *in vivo* toxicity compared to the L-BMAP18 [4]. In order to maintain the stability and reducing the toxicity we designed the Pro-D-BMAP18, an inactive D-BMAP18 obtained by the addition of negatively charged pro-sequence, that should be cut off in the lungs by the neutrophil elastase released during infection. The inactivity of the pro-drug was verified as the loss of its antimicrobial activity and in parallel it showed a remarkable reduction of the *in vitro*cytotoxicity. We tested its elastase-dependent *in vitro* activation using a neutrophil-like cell line. The activation of the pro-drug restored the original antimicrobial activity in vitro. The examination of its activation and activity in CF patients' sputum and the observation of its protective activity *in vivo* in a murine model of pulmonary infection will allow to understand the therapeutic potential of this compound in the treatment of CF pulmonary infections.

[1] Gillanders et al. (2011) Therapy 8(6), 645–660
[2] Zang et al. (2005) Antimicrobial agents and chemotherapy 49(7), 2921-2927
[3] Skerlavaj et al. (1996). The journal of biological chemistry 271(45): 28375-28381
[4] Benincasa et al. (2003). Peptides 24: 1723-1731
[5] Mardirossian et al. (2016). Amino acids 48(9):2253-2260
[6] Mardirossian et al. (2017). Frontiers in Chemistry

24/08/2017 – 26/08/2017 Copenaghen- Denmark

7°International Meeting on Antimicrobial Peptide (IMAP 2017) Poster presentation: "Optimization of the peptide D-BMAP18 for the *in vivo* treatment of CF pulmonary infections"

23/11/2016 – 25/11/2016 Verona- Italy

XIV Convention d'autunno dei ricercatori in fibrosi cistica Poster presentation: **"**In vitro evaluation of Pro-D-BMAP18 for the treatment of cystic fibrosis- related pulmonary infections"

30/08/2016 – 02/09/2016 Leipzing- Germany

6° International Meeting on Antimicrobial Peptide (IMAP 2016) Poster presentation:"*In vitro* and *in vivo* evaluation of BMAP-derived peptides for the treatment of cystic fibrosis-related pulmonary infections"

Training

06/05/2021 – 06/05/2021

Training for Infinium assay

Training di 3 ore relativo alla chimica dell'infinitum assay con un'overview sull'infinitum methylation array e sull'analisi dei dati mediante GenomeStudio

08/03/2021 – 09/03/2021

Advanced Nanopore Training

Il training è durato tre giorni ed è stata fornita una panoramica generale della tecnologia di sequenziamento di Oxford Nanopore.
Nei primi due giorni è stato progettato e eseguito un protocollo di sequenziamento per ligazione con successivo caricamento della libreria nella flowcell dello strumento (PromethION) e valutazione della qualità e dell'andamento dell'analisi. Sono stati introdotti anche i flussi di lavoro del base calling e del software di analisi Epi2ME.

L'ultimo giorno (eseguito separatamente il 7/5/2021) è stato interamente incentrato sull'analisi dati e sui software per analisi primaria e secondaria dei risultati ottenuti.

14/12/2020 – 15/12/2020

Training for MiSeq DX RUO mode

La durata del training è stata di 1.5 giorni ed è stato incentrato sia su argomenti teorici che pratici.
Per quanto riguarda la parte teorica; è stata fatta una overview iniziale sulla tecnologia di sequenziamento Illumina e sul protocollo da seguire per il setup della corsa. Successivamente è stato illus trato il funzionamento del local run manager. Per terminare ci si è concentrati sull'analisi dei dati e sugli elementi da considerare per valutare la bontà di una corsa.
Nella parte pratica è stata eseguita una corsa di sequenziamento di librerie precedentemente preparate in laboratorio

Competenze comunicative e interpersonali

Competenze sociali Ottima attitudine alla gestione dei rapporti interpersonali. Ottime capacità di lavoro in gruppo e di adattamento, acquisite in contesti pregressi di lavoro in laboratorio e buona capacità di integrare e collaborare con figure professionali differenti.

Competenze organizzative

Organizzazione e gestione del lavoro Capace di pianificare il lavoro, definendo priorità e scadenze. Buona organizzazione del lavoro sia in solitario che all'interno di un team. Oytime capacità di problem-solving maturate durante le esperienze di dottorato e di assegni di ricerca. Ottime doti decisionali e senso del rispetto.

Patente di guida

Patente di guida: B

Autorizzo il trattamento dei miei dati personali presenti nel CV ai sensi dell'art. 13 d. lgs. 30 giugno 2003 n. 196 - "Codice in materia di protezione dei dati personali" e dell'art. 13 GDPR 679/16 - "Regolamento europeo sulla protezione dei dati personali".

