Curriculum vitae et studiorum

ISTRUZIONE E FORMAZIONE

Iscrizione all'albo - sezione A dell'Ordine Nazionale dei Biologi (ONB)

08 Settembre 2021

Numero di iscrizione: AA_090272

Laurea Magistrale in Scienze Biologiche con indirizzo in Diagnostica Molecolare (LM- 6) con votazione 110/110 e lode

Gennaio 2018 – febbraio 2021

Università degli Studi di Napoli "Federico II" (Napoli, Italia)

Tesi sperimentale in Genetica (Relatore Prof.ssa Serena Aceto; Correlatore: Dott.ssa Enza Lonardo) dal titolo: *"Targeting di LAMC2 tramite la tecnologia CRISPR/Cas9 in cellule tumorali pancreatiche"*

Attestato PF24

Febbario 2020

Università degli Studi di Napoli "Federico II" (Napoli, Italia)

Pedagogia scolastica (6CFU), Psicologia per l'insegnamento (6CFU), Antropologia culturale (6CFU), Pedagogia sperimentale (6CFU)

Laurea Triennale in Scienze Biologiche con indirizzo Fisiopatologico (L-13) – con votazione 107/110

Ottobre 2013- dicembre 2017

Università degli Studi di Napoli "Federico II" (Napoli, Italia)

Tesi sperimentale in Patologia Generale e Veterinaria (Relatore Prof. Franco P. Roperto) dal titolo: *"L'espressione di Eras nei tessuti equini"*

Istruzione Secondaria Superiore - Ordine Scientifico con votazione 81/100

Settembre 2008 – luglio 2013

Liceo Scientifico statale "Elio Vittorini" (Napoli, Italia)

CONVEGNI & CONGRESSI

1. Title: *LAMC2 drives tumorigenicity and metastasis in pancreatic ductal adenocarcinoma*.

Name of the conference: 2nd IBBR Workshop. Type of event: workshop. City of the publishing body: Naples, Italy. Date of the event: 25-26 October **2021**. Your role: **abstract.**

LAMC2 drives tumorigenicity and metastasis in pancreatic ductal adenocarcinoma

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ABSTRACT

Pancreatic ductal adenocarcinoma (PDAC) is a leading cause of cancer-related mortality with limited therapeutic options. Cancer stem cells (CSCs) are key player in PDAC chemoresistance, tumor initiation and metastatic spreading, but the mechanism through which they acquire metastatic traits is not well understood. Hence, targeting the CSC niche and their plasticity could be a complementary therapeutic strategy against cancer. Laminin subunit-γ-2 (LAMC2) is an epithelial basement membrane protein, which controls cell motility and adhesion and is widely expressed in the majority of human tumors. However, its role in PDAC remains largely unknown. Here, we propose LAMC2 as a key driver of PDAC stemness and tumorigenicity.

In several patient cohorts we observed that high levels of LAMC2 significantly correlated with shorter overall survival. In addition, the tissue microarray analysis on PDAC sections revealed prognostic significance of LAMC2 expression in tumor with high grade of aggressiveness (i.e., G2 and G3). To determine the role of LAMC2 in sustaining tumorigenicity, we knocked down it in patient-derived xenografts (PDX) cells using lentiviral shRNA constructs. The silencing of *LAMC2* resulted in decreased self-renewal, invasiveness and gemcitabine resistance both *in vitro* and *in vivo*. To track the LAMC2 tumor cell population in an intact environment we engineered primary PDAC cells that carry EGFP cassette knocked in the *LAMC2* locus through the CRISPR-Cas9 technique. *In vivo* experiments revealed increased tumorigenicity of the LAMC2High-EGFPHigh cells respect to LAMC2Low-EGFPLow cells, while RNA-seq data obtained from cells extracted from tumors confirmed a gene program similar to that of highly metastatic stem cells and that they initiate and propagate both the primary tumor and the metastasis to recipient mice very efficiently compared to their counterpart. In addition, Gene Set Enrichment Analysis (GSEA) indicates that *LAMC2* is enriched in the squamous molecular subtype of pancreatic cancer, which is the one associated with the worse prognosis.

In conclusion, we identified a highly metastatic subpopulation of cancer stem cells, characterized by high levels of LAMC2. Strategies aimed at targeting the LAMC2 population may be effective in reducing tumor aggressiveness in combination with conventional therapy.

2. Title: *LAMC2: new player in stemness and tumor progression in pancreatic cancer*.

Name of the conference: AACR Pancreatic Cancer Virtual Congress. Type of event: Congress. City of the publishing body: Virtual Meeting. Date of the event: 29-30 September **2021.** Your role: **abstract.**

LAMC2: new player in stemness and tumor progression in pancreatic cancer

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ABSTRACT

Pancreatic ductal adenocarcinoma (PDAC) is a devastating and essentially incurable disease, typically characterized by high chemoresistance and metastatic spread attributable to cancer stem cells (CSCs). This subpopulation is critical for tumor initiation and recurrence, but the mechanism through which they acquire metastatic traits is not well understood. Hence, targeting the CSC niche and their plasticity could be a complementary therapeutic strategy against cancer. Laminin subunit-γ-2 (LAMC2) is an epithelial basement membrane protein, which controls cell motility and adhesion and is widely expressed in the majority of human tumors. However, its role in PDAC remains largely unknown.

In several patient cohorts we observed that high levels of LAMC2 significantly correlated with shorter overall survival. In addition, the tissue microarray analysis on PDAC sections revealed prognostic significance of LAMC2 expression in tumor with high grade of aggressiveness (i.e., G2 and G3). To determine the role of LAMC2 in sustaining tumorigenicity, we knocked down it in patient-derived xenografts (PDX) cells using lentiviral shRNA constructs. The silencing of *LAMC2* resulted in decreased self-renewal, invasiveness, tumorigenicity and gemcitabine resistance both *in vitro* and *in vivo*. To identify or track the LAMC2 tumor cell population in an intact environment we engineered primary PDAC cells that carry EGFP cassette knocked in the *LAMC2* locus through the CRISPR-Cas9 technique. Analysis of LAMC2-EGFP+ cells isolated from tumor demonstrated that these cells express a gene program similar to that of highly metastatic stem cells and that they initiate and propagate both the primary tumor and the metastasis to recipient mice very efficiently compared to their counterpart. In conclusion, we identified a highly metastatic subpopulation of cancer stem cells, characterized by high levels of LAMC2. Strategies aimed at targeting the LAMC2 population may be effective in reducing tumor aggressiveness in combination with conventional therapy.

Keywords:

Pancreatic ductal adenocarcinoma (PDAC), Laminin γ2 (LAMC2), Cancer stem cells (CSC), metastasis