GESINAS - ImmunoTools Award 2021

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Assessing the biological activity of pancreatic cyst fluid and its role in the development of pancreatic cancer

Background

Pancreatic cancer is one of the worst prognosis cancers with a 5-year survival rate of approximately 3%. This rate has improved over the past 40 years or so for cancers such as breast or prostate, which would be more prevalent and receive more research funding, but for pancreatic cancer this rate has remained low with very little improvement. The poor survival rates we see in this cancer are attributed to the rarity of the cancer and a lack of funding into research, but also to the vague nature of the symptoms that are associated with pancreatic cancer. Symptoms such as abdominal pain, weight loss or fatigue, which the average person would experience from time to time, cause patients to overlook these signs and so present to their GP with worsened symptoms and therefore a later stage of cancer development.

Pancreatic cystic lesions (PCLs) are fluid-filled structures found within or on the surface of the pancreas. There are many different subtypes of pancreatic cysts, each with their own rate of malignant transformation. While many cysts are benign and show no malignant potential, others, such as intraductal papillary mucinous neoplasms (IPMNs), possess the ability to undergo malignant transformation and can be regarded as precursor lesions of pancreatic cancer. IPMNs are the most common pre-malignant pancreatic cyst, are notoriously unpredictable and are therefore the most challenging to stratify based on risk. There are currently a number of clinical guidelines (2018 European evidence-based guidelines (EEG), 2017 International Association of Pancreatology Fukuoka guidelines, 2015 American Gastroenterological Association (AGA) guidelines) that aim to help stratify the risk of IPMNs undergoing malignant transformation. However, the fact there are differing consensus guidelines in use is indicative of the imperfect state of knowledge regarding pancreatic cysts and pancreatic cancer and the urgent need for improved biological characterisation of these lesions.

Pancreatic cyst fluid (PCF) is known to contain many factors, including proteins such as chemokines and cytokines. PCF is believed to be secreted by the cells lining the cyst, however, this has not yet been definitively shown and as such the origin of these factors remains unknown. Preliminary work from our lab has revealed that the PCF

may be biologically active, and that exposure of normal pancreatic cell lines to PCF obtained from low-risk and high-risk cysts has a differential effect on cell line proliferation.

T cell infiltration is known to be poor in pancreatic tumours, making them incapable of eliciting antitumor immunity. As such, pancreatic tumours are considered to be “immunologically cold”. However, recent studies have shown that when T-cell immunity in pancreatic cancer is sufficiently induced, T cells become effective weapons. The presence of certain chemokines within the PCF may play a role in the poor recruitment of T cells to pancreatic tumours. Furthermore, the factors within the PCF may have a negative effect on T cell activation, maturation and metabolism.

Objective
Examine the influence of both pancreatic cancer cell line and normal pancreatic cell line conditioned media on polarised and unpolarised T cell cytokine production by ELISA and flow cytometry.

Methodology
T cells will be isolated from healthy blood and polarised to various T cell linages using rh cytokines. Both polarised and unpolarised T cells will be treated with pancreatic cancer cell line and normal pancreatic cell line conditioned media. The cytokine production of the T cells will be examined ELISA, while T cell profiling will be carried out using flow cytometry.

GESINAS-ImmunoTools-Award Statement
I am actively involved with Junior Einstein’s Science Club, an Irish franchise which delivers hands-on STEM education to young children. In collaboration with Junior Einstein’s and the United Nations, I am presently involved in the recording of a series of STEM education videos for children in third world countries which will be distributed free of charge in an effort to encourage science education in these areas. I am also in receipt of a ‘Leaders in Learning’ grant from Dublin City council for my contributions to education in the local community. In collaboration with the Ballyfermot-Chapelizod Partnership I deliver online webinars to third level students and visit local schools to speak about my research and student life.

GESINAS - **ImmunoTools** AWARD for **Laura Kane** includes 16 reagents

FITC - conjugated anti-human CD4

PE - conjugated anti-human CD8

APC - conjugated anti-human CD3

recombinant human rh IL-12, rh IL-4, rh IL-6, rh IL-2, rh TGFB-3

human ELISA-set: IFN-gamma, TNF-a

DETAILS more AWARDS