BDIAP Glasgow 2020 fellowship report

Name of bursary recipient: Lamia Sabry Abo Elnasr

Year Bursary awarded: 2019.

Trainee grade and institution: Master's degree in pathology, pathology teaching assistant position, Pathology Department, Faculty of Medicine, Menoufia University.

General background of Project:
Despite significant advances in diagnosis, treatment, and care, the prognosis of colorectal cancer (CRC) has not improved satisfactorily. Immunosuppression within the tumor micro-environment has become an important and promising treatment target. In immune cells, CD73 dephosphorylates and converts extracellular AMP into adenosine, which binds the A2A adenosine receptor (A2AR). Preclinical studies have identified that blockade of this interaction, which induces an immunosuppressed niche in the tumor microenvironment, represents a potential novel treatment strategy through limiting tumor initiation, growth, and metastasis. The immunohistochemical (IHC) assessment of CD73 and A2AR expression and its correlation with clinicopathological prognostic parameters, however, have yet to be thoroughly investigated in CRC. This study aimed to determine IHC expression levels of CD73 and A2AR and to test their correlation with clinicopathological parameters in CRC.

Topic of research: Was this chosen by you? Yes

If so, what attracted you to it and why?
I have had a research project investigating the role of PD-L1 and CTLA-4 in colorectal cancer. Through that project, I have read papers discussing other tumor microenvironment related biomarkers that had a role in regulating anticancer immune response and also had a promising future in target immunotherapy in cancer. Between those biomarkers, I noticed the great synergistic role of CD73 and A2ar that were not investigated simultaneously in colorectal cancer.

Department where the research was carried out?
Pathology Department, Faculty of Medicine, Menoufia University.

A summary of the project

What were the aims and objectives? What methods were used? What results did you get? Were they what you expected?

Objectives

In immune cells, CD73 degrades adenosine triphosphate into adenosine, which binds the A2A adenosine receptor (A2AR). This interaction potently inhibits immune responses against cancer. However, the expression of these two markers has never been studied in colorectal cancer (CRC) simultaneously.

Methods

We evaluated the immunohistochemical expression of CD73 and A2AR in tumor cells and stromal lymphocytes in tissue microarrays collecting tumor and adjacent nontumor tissue specimens of 103 patients with CRC. Each of CD73 and A2Ar staining was evaluated as staining intensity and percentage of positivity which were then multiplied and reported as histoscore (H-score).

Results

H-score values of CD73 and A2AR in tumor tissues were significantly higher compared to matched adjacent nontumor tissues. High H-score values of both CD73 and A2AR in tumor cells were significantly correlated with advanced stage and higher tumor grade. Both CD73 and A2ar expression levels in tumor cells were positively correlated in tumor cells. Moreover, univariate analysis showed that high expression levels of CD73 and A2ar were significantly associated with poor overall survival and short recurrence free survival. However, High CD73 stromal expression was significantly correlated with better overall survival and prolonged recurrence free survival. Multivariate analysis confirmed that both markers were independent predictors of prognosis in CRC patients.

Conclusion

CRC cases harboring high levels of CD73 and A2AR are more liable for tumor progression. Therefore, these markers could be used as predictors for high-risk patients, thus, to optimize individualized treatment for this group.

Your role?
My role in the project started from initiating the idea of research project, carrying out the methodology plan, evaluating markers' expression, performing statistical analysis till reporting the results.

What did you learn from this experience?
Being the principal investigator in this research project has taught me so many values and skills. I have learnt how to form, test my hypotheses and how to plan for each step with time management. I have acquired hands-on experience in methodology techniques such as tissue microarray. I have also gained a deeper understanding in histopathologic and immunohistochemical evaluation. I have learnt how to report findings.

You may want to mention your supervisor and their role as this project may be part of a larger project.
I want to express my deep great gratitude to my supervisors who helped me through the research methodology steps; Prof Asmaa Gaber Abdou, Prof Hala Said ElRebey, Dr Asmaa Shams ElDein.

What proportion of the project was histopathology?
My project included tissue microarray technique, histopathologic and immunohistochemical evaluation.

Has this experience changed your views about Histopathology and research? If so, in what way?
Yes, to better and deeper understanding and enthusiasm to learn more, explore more and more.

Did COVID-19 impact your research?
Fortunately, Covid-19 did not impact my project because I have finished the methodology in early February 2020 and after that I have reported and interpreted results.

Did you enjoy the meeting?
Yes, I am still listening to lectures till this moment so that I could not miss these great educational opportunities.

What were the highlights for you? What would you like to see more of and less of?
Computational pathology, digestive disease pathology and breast pathology. Indeed, I would like see much of all that belongs to BDIAP.'

How did your presentation go? What did you enjoy about preparing the presentation and delivering it? What did you not enjoy about it?
It was an interesting experience for me and I was extremely excited during preparing the presentation and through my trials to deliver it as proper as I wish.