MTT assay: As shown in Fig 2, desired schiff base prevented the growth of cancer cells in time and dose dependent manners with an IC_{50} about 400 µg/ml.

Flow cytometry analysis: Flow cytometry result show that with increasing concentration of treatment SubG1 peak shows a significant increase from 16.2% to 94.8%. The SubG1 peak in IC_{50} have been reported of about 69%.

Discussion: Lately, the synthesis of ligands and metal complexes for medical and industrial applications has attracted much attention. So far, many studies have been done in the field of anti-cancer effects of various complexes of Schiff bases. Ssynthesized copper (II) complexes of schiff bases are able to prevent the growth of HepG2 cancer cells. Farag and et al studied proapoptotic effects of Cu, Mn, Zn complexes of schiff base on HepG2 cells and showed that Zn (II) and Cu (II) complexes have a noticeable antiproliferative (IC50 = 4.6 lg/mL) and proapoptotic effect on HepG2 cells. However, some of these compounds inhibited viability of cells and induced apoptosis through activation of caspase pathway. Findings from another study showed that some complexes of morpholine Schiff bases have antiproliferative effect on MCF7 cells. IC50 of Mn(L1)Cl, Cu(L1)Cl and Zn(L1)Cl were about 24.54, 37.58 and 10.94µg/ml, smaller than Mn2+ Complex of the N, N′-dipyridoxyl (1, 2-diaminobenzene) Schiff Base in the present study.

Conclusions: The Mn2+ complex of the N, N′-dipyridoxyl (1, 2-diaminobenzene) Schiff base showed anti-proliferative activity on MCF7 cells and induced apoptosis in these cells.

Keywords: Schiff base, Mn2+ complex of the N, N′-dipyridoxyl (1, 2-diaminobenzene), Antiproliferative, Apoptosis

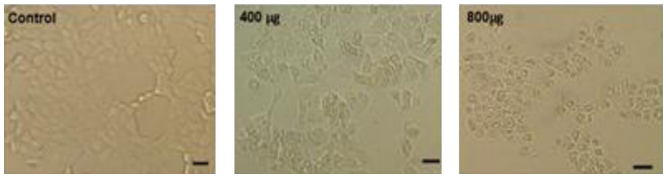

Fig. 1. Morphological alterations in MCF7 cells at different concentrations of Schiff base (0,400 and 800 µg/ml). Reduction in the number, size and shape of the cells is visible (Scale bar: 20µm).

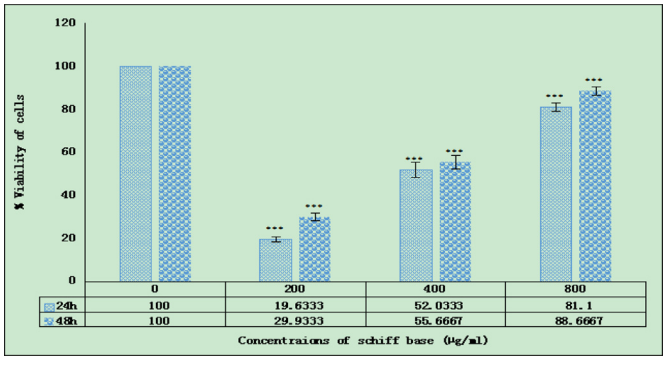

Fig. 2. Anti-proliferative effect of Mn2+ complex schiff base on MCF7 cells after 24 and 48h treatment. Results are expressed as mean ± SD (***P<0.001 is significant).

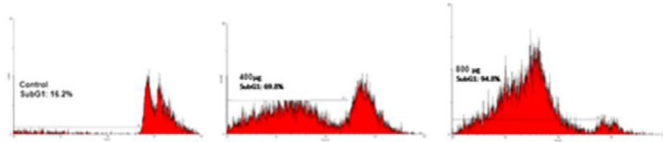

Fig. 3. Flow cytometry assay of MCF7 cells that treated with different concentration of Schiff base. The SubG1 peak increased with increasing concentration of treatment.

The prognostic value of biomarkers in esophageal squamous cell carcinoma in Iranian population

Mohammadreza Mirinezhad [a], Narjes Khalilipour [b], Reza Raoofian [a,c], Majid Alizadeh [d], Mohammad Reza Abbaszadegan [b,e,*]

[a] *Innovative Medical Research Center, Islamic Azad University, Mashhad Branch, Mashhad, Iran* [b] *Medical Genetics Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran* [c] *Legal Medicine Research Center, Legal Medicine Organization, Tehran, Iran* [d] *Department of Medical Parasitology and Mycology, Mashhad University of Medical science, Mashhad, Iran* [e] *Division of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran*

E-mail address: Abbaszadeganmr@mums.ac.ir

Extended Abstract

Introduction: Esophageal cancer (EC) is the eighth most common type of malignancy and is the sixth leading cause of cancer-related mortality worldwide. The average 5-year survival rate is only seen in 35-45% of patients. In Iran esophageal cancer is the 4th common cancer in women and sixth cause of death in men. The incidence rate of EC varies considerably from one country to another. The high-risk area for ES is extending from northern Iran to north-central China (Asian belt of EC).

EC is considered as growing health concern and its incidence is expected to be increased by 140% by 2025.

Two main forms of esophageal cancer are squamous cell carcinoma (ESCC) and adenocarcinoma (ADC). More than 90% of all diagnosed esophageal cancers in Iranian patient are the squamous cell type.

Several risk factors have been investigated as possible etiologic factors for esophageal squamous cell carcinoma. In Iran, many risk factors contributing to the development of squamous cell carcinoma of the esophagus are evaluated. Alcohol is rarely consumed by men in Northeastern Iran, neither women. The proposed risk factors in Iranian patients include a low intake of fruits and vegetables, the consumption of very hot beverages, exposure to carcinogens due to opium consumption, tobacco smoking, nass chewing and low socio-economic status may play roles in development of ESCC.

Moreover genetic susceptibility was suggested to play an important role in pathogenesis of ESCC. So, we can consider ESCC as a complex and multifactorial disease. Several studies have conducted to find out biomarkers for ESCC. In this review we have listed some important biomarkers of ESCC patient in Iranian population.

In this regard, abnormal activity of major cell signaling pathways such as Apoptosis, Notch and Wnt plays important roles in ESCC progression. Dysregulation of some of these important signaling pathways is involved in tumorigenesis.

Table 1 Important biomarkers in ESCC patient in Iran. We used DAVID pipeline to identify pathways that these biomarkers are involved.

Wnt, Notch and Apoptosis signaling pathways play an important role in cell fate decision during development. Besides, Wnt signaling is an important pathway that is involved in determination of cellular development, self-renewal, and fate, and also tumor development and progression.

As a result, based on the fact that no standard early diagnostic guideline has been proposed to date and current therapeutic modalities are not efficient, detection of specific biomarkers could be of great value in the early diagnosis ESCC. Therefore, in this review

Table 1 Important biomarkers in ESCC patient and their important role.

Biomarkers	Wnt signaling pathway	Notch signaling pathway	Apoptosis signaling pathway	Roles in ESCC
HEY1		✓		Over-expression of HEY1 in ESCC is correlated to different indices of poor prognosis
HEY2		✓		Over-expression of HEY2 in ESCC is correlated to different indices of poor prognosis
CD44	✓		✓	*Up-regulation of CD44 in ESCC samples*
MDM2	✓	✓	✓	
HES1	✓	✓		*HES1 under-expression was significantly correlated with tumor depth of invasion*
MUC1	✓		✓	Specific MUC1 splice variants are correlated with tumor progression in ESCC
SALL4	✓		✓	SALL4wasover-expressed and have a significant correlation with invasion and metastasis in ESCC
SOX2	✓	✓	✓	SOX2 was over-expressed and have a significant correlation with invasion and metastasis in ESCC
Msi1	✓	✓	✓	Msi1 was significantly over-expressed in 41.5% of ESCC tumor sample
MMP2	✓		✓	MMP2 was significantly over-expressed and it could be used as specific diagnostic, prognostic and therapeutic biomarker for ESCC
HLA-G			✓	HLA-G was significantly over-expressed and it could be used as specific diagnostic, prognostic and therapeutic biomarker for ESCC
XRCC5	✓		✓	XRCC5 was significantly over-expressed and it could be used as specific diagnostic, prognostic and therapeutic biomarker for ESCC
MAML1	✓	✓		MAML1 was significantly over-expressed in ESCC patient and significantly associated with lymph node metastasis and the surgical staging of tumor
TWIST1	✓	✓	✓	TWIST1 was significantly over-expressed in ESCC patient and associated with lymph node metastasis and the surgical staging of tumor
p53/P21	✓	✓	✓	p53 and p21 expression play an important role in ESCC development in northeastern Iran(36)
GSTP1			✓	Exposure to some cigarette related pro-carcinogens could activate GSTP1 domain, which may responsible for the increased susceptibility to ESCC(37)

we have clarified the prognostic value of these biomarkers and their association with three signaling pathways.

Conclusion: These biomarkers had a strong prognostic value in ESCC. The rising incidence and poor prognosis of ESCC in Western countries have intensified research efforts for developing earlier methods of disease detection. It is well recognized that early diagnosis of cancer can provide the means for the full recovery of patients. However, conventional methods of cancer screening are often invasive and expensive. Sensitivity and specificity of these methods are also insufficient for the diagnosis of cancer at earlier stages.

In addition, we found some other related biomarkers such as Brg1, LAGE1, p21, MAGE-A4, NY-ESO1, P16, D44V3, IL-10, TGF-beta and VEGF, showed important effects on survival, disease progression and clinicopathological characteristics of ESCC patients.

Actually, alteration in the expression of p53 tumor-suppressor protein is an event that occurs frequently in human cancer, but the practical implications of this phenomenon are yet to be fully exploited. It has been shown that the p53 and p16 tumor suppressor genes are involved in the cell cycle control and protecting cells exposed to DNA-damaging agents. Moreover, SOX2 is an important key transcription factor involved in self-renewal and pluripotency characteristics of undifferentiated ESCCs. In addition, it is a member of master transcriptional complex consisting of OCT4/SOX2/NANOG which can reprogram differentiated cells to induced pluripotent stem cells.

Nonetheless, TWIST is among the proteins that induce and promote epithelial mesenchymal transition (EMT). Up-regulation of TWIST1 has been suggested to enhance invasion and metastatic ability of various types of tumor cells including ESCC.

CD44 is a member of the cell adhesion molecules family. Naturally, CD44 influences cell motility, migration, and adhesion, while in tumor cells it leads to tumor invasion, progression, and metastasis.

Although significant advances have been made in the treatment of ESCC, this aggressive malignancy commonly presents as a locally advanced disease with a poor prognosis. Despite the advances in the detection of premalignant pathology and newer preventative strategies, these biomarkers are of high significance in disease prognosis. With a poor prognosis, EC poses a great burden on societies, particularly Eastern Asian countries. However, so far, no clinically approved biomarker has been identified for an early medical intervention.

Based on our study, we find that some biomarkers are correlated with late stage, depth of invasion and unfavorable response to chemotherapy such as LgR5. These markers cannot be recommended for clinical application due to absence of sufficient clinical investigations and scientific reports and undetermined specificity and sensitivity in comparison with standard methods. This study can be considered as a source of Biomarkers evaluation, which is a useful and valuable means for cancer management. Overall, biomarker analysis can lead to novel biomarker panels which can be useful in order to increase the overall survival rate.

Keywords: Esophageal squamous cell carcinoma, Prognostic value, Biomarkers

Anti-metastatic effect of polysaccharide extracted from brittle star *Ophiocoma erinaceus* on human cervical cancer cells in vitro

FarzanehSalek Abdollahi [a], Javad Baharara [b], Najme Nikdel [a], Elaheh Amini [c,*]

[a] *Faculty of Biological Science, Mashhad Branch, Islamic Azad University, Mashhad, Iran* [b] *Department of Biology, Research Center for Applied Biology, Mashhad Branch, Islamic Azad University, Mashhad, Iran* [c] *Department of Animal Biology, Faculty of Biological Sciences, Kharazmi University, Tehran, Iran*

E-mail address: elah.amini73@gmail.com