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The importance of the CD133 marker in predicting esophageal cancer

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Abstract
Esophageal carcinoma is an assailant cancer, with poor forecast and short existence rates. While analysis and therapy have enhanced noticeably, more qualified predictive factors are instantly wanted to avoid postoperative reappearance and metastasis. The presence of stemness genes and clinical outcome have been linked in several studies because cancer stem cells are a major driving force for growth evolution. The extrapolation of stemness markers in esophageal tumor leftovers remains contentious.

Keywords: CD133, marker, poor forecast, enhanced noticeably

Introduction
Gastrointestinal cancer (GI)
Cancer is the nonstandard growing of cells that incline to thrive in an unrestrained system. More than 32.5 million persons in the world are affected by diverse types of cancer; Esophageal cancer accounts for almost a percentage (465000) of it. Approximately 80% of the cases documented come from less developed parts of the world (Sardana, Chhikara, Tanwar, & Panghal, 2018) [57]. It is the second main reason of demise in the US and a chief reason of mortality and morbidity international (Glumac & LeBeau, 2018) [16, 17]. The GI, counting the esophagus, stomach and intestine. It has the main cancer occurrence and malignance associated mortality in the body and is influenced by heritable and ecological influences (Bishak, Payahoo, Osatdrahimi, & Nourazarian, 2015) [6].
Gastric tract tumor, comprising oral, pharyngeal, esophageal, gastric, and colorectal malignances, are amongst a topmost 10 mutual sarcomas in world (Rassouli, Matin, & Saeinasab, 2016) [53].
(GI) theatres dominant part in the preoccupation, spreading, absorption, and evacuation of flavonoids, which eventually explain the health belongings of the bioactive. The facets are moderated via the communications of flavonoids with added nutritional machineries, conservational features, crowd, and GI micro biota (Oteiza, Fraga, Mills, & Taft, 2018) [47]. Esophageal and intestinal cancers are greatest mutual in the non- manufacturing nations, while colorectal malignance is amain gastrointestinal distortion in weste states (Rozen, 2004) [54]. The problem of GI cancer is cumulative in Asia because of elderly, growth of the populace and the hazard aspects comprising smoking, obesity, changing lifestyle and high occurrence of *H pylori*, HBV and HCV (Mohamad Amin, Mohsen, & Ahmad Reza, 2015) [39]. Accruing evidence specifies that GI malignances progress meanwhile the gathering of heritable and epigenetic modifications, which are prejudiced by steward resistance, regime, and ecological and bacteriological introductions (Song, Garrett, & Chan, 2015) [62]. Almost 100 trillion microbes reside the human GI and show significant characters in healthiness situations and sicknesses, comprising sarcoma (Mima *et al*., 2017) [36].

Esophageal cancer (EC)
This is an antagonistic disease and unique of the peak mortal malignances global with poor survival and incomplete treatment choices (B. Li *et al*., 2017). Furthermore, the 8 most communal cancer universal and the 6 chief source of cancer- correlated deceases widespread (X.-M. Li, Wang, Zhu, Zhao, & Ji, 2015) [30] with a 5-year survival rate of ~14% (Ferlay *et al*., 2010; Pennathur, Gibson, Jobe, & Luketich, 2013) [15, 51]. EC a thoughtful virulence with respects to transience and prediction (Napier, Scheerer, & Misra, 2014) [43].

Subsequently the early 1970s, the frequency of EACs has amplified melodramatically in most Western populations. In disparity, the rate of esophageal squamous-cell cancer has reduced in these same populaces (Thrift, 2016) [66].

This cancer typically about (3-4) times more mutual in men than in women (Torre, Siegel, Ward, & Jemal, 2016) [67] and frequency of this cancer is more in fewer industrialized and emergent states. Statistically noteworthy relationship was not start between uniform occurrence and death rates of this disease, and Human Development Index and its magnitudes, excluding for life expectation at natural (Pakzad *et al*.2016) [82].

The designs and leanings have been exposed to change decidedly by the two focal histologic subtypes, esophageal adenocarcinomas (EACs) and squamous cell carcinomas (ESCC) (Colquhoun *et al*., 2015) [9]. EAC is the sixth important source of death by cancer global and has been intensely growing in prevalence over the past decade (R. Liu, Li, Hylemon, & Zhou, 2018) [31]. The gastroesophageal reflux disease GERD reflect a chief menace reason for EAC, and the UK has the uppermost frequency of EAC internationally (Markar *et al*., 2018) [35]. The two chief kinds of EC, EAC and ESCC, have suggestively diverse structures in risk factors, etiology and epidemiology (Arnold, Soerjomataram, Ferlay, & Forman, 2015) [9].

Regional incidence rates of EC

Current esophageal cancer incidence and humanity trends have been examined using numbers accessible from the WHO mortality database, the GLOBOCAN 2012 database and the Cancer Frequency in Five Islands list achieved by the Worldwide Agency for Study on Cancer (B. Li *et al*., 2017). ESCC is a shared neoplasm which occurrence displays an collective drift in most people (Khorshidi, Taghipour, Yousefi, & Dehghan, 2018) [26] The so-called "Asian Esophageal Cancer Belt" covers zones such as Turkey, Iran, Kazakhstan and northern and central China, with an projected ESCC of more than 100 cases/100000 person-years. Added area through high frequency of squamous cell carcinoma is southeastern Africa, by comparable rates to those observed in Eastern nations (Zhang, 2013) [77] (Jemal *et al*., 2009) [24].

Nearly 70% of global esophageal tumor suitcases take place in China, with esophageal squamous cell carcinoma (ESCC) existence the histopathological procedure in the massive popular of bags (>90%) (Xu, Yu, Chen, & Mao, 2012) [76].

The regularity of esophageal adenocarcinoma (EAC) consumes climbed 600% above the latest 30 ages. With a 5-year existence amount of ~15%, the documentation of fresh healing boards for EAC is critically significant (Dulak *et al*., 2013) [10].

The load from EAC is predictable to increase intensely crosswise high-income republics also has previously or else will better ESCC commonness in the pending an age, specially between men (Arnold, Laversanne, Brown, Devesa, & Bray, 2017) [4]. Vast geographical difference is an epidemiological typical of oesophageal disease, with the maximum commonness taxes experiential in Eastern Asia and in Eastern and Southern Africa and the nethermost charges experiential in Western Africa. The variation is to the command of extra than 21 periods amid the lowest-incidence and the highest-incidence republics. While the prevalence of SCC is aggregate universally, its numbers tolls are lessening in the USA and a few European states. Nonetheless, the diminution in the occurrence of SCC in these republics has been escorted by a noticeable surge in adenocarcinoma incidence tariffs (Gupta, Bhardwaj, & Bhagat, 2017) [19].

Identify and therapy of esophageal

A defined valuation for adapted conduct be contingent on the correctness of the first analysis. Learning about people's faith in inclusive plus proper white-light, iodine discoloration, and narrow-band imaging endoscopic procedures. These devices have limitations in terms of adding to the hostile countryside and the potential hazards associated with the route. These restrictions include hiccups in comprehensive growth specification to allow for whole-growth excision, irritation and distortion variety, and step resolution, among other things (Wu *et al*., 2018) [75].

Mutual imaging modalities recycled in performance comprise calculated tomography, endoscopic ultrasound and positron release tomography shots. Present behavior choices comprise multimodality remedial supports of recent behavior encompass hospital, pollution and chemotherapy. Cancer indicators of esophageal malignancy are a proceeding part of investigation that might possibly principal to former judgment as healthy as singing a share in measuring polyp reply to rehabilitation.[11] Surgery is the main form of conduct, but the survival is poor, particularly for patients with locally progressive esophageal cancer [129]. Multimodal handling, which includes chemotherapy, radiation treatment surveyed by surgical resection or starved of surgical resection, in variable orders remains the main mode of dealing for most patients (Abbas & Krasna, 2017) [1]. The rehabilitation and organization of esophageal cancer have better in topical

an age without the application of harmless procedures for esophagogastric anastomosis (Nakashima *et al*., 2016) [42] and unimportantly invasive esophagectomy with radical lymphadenectomy (Saeki *et al*., 2018), by way of the introduction of neoadjuvant treatment (Nakashima *et al*., 2018) [41]. EC has a deprived forecast, directing patients detailed CSC signals may recover medical consequence in the nearby upcoming. Meanwhile, cautious investigation of patient's detailed polyp may central to a handmade remedy method, where together CSC and the unpackaged cancer can possibly be devastated primary to a further acceptable importance for EC patients (Wang, Plukker, & Coppes, 2017) [72].

Risk factor of EC

In surveys of EC, smoking, drinking hot tea, eating a lot of red meat, having weak oral strength, eating little fresh fruit and vegetables, and being in a low socioeconomic position have all been linked to a higher risk of ESCC, according to the findings (Zhang, 2013) [77].

Risk effects for the growth of ESCC contain inferior socioeconomic position, feasting of tobacco, alcohol, hot brews, and nitrosamines (Huang & Yu, 2018) [21]. Furthermore, micronutrient shortages have also been connected to the progress of ESCC. These contain vitamin C, E, and folate. With deference to EAC, risk agents comprise Barrett's esophagus, GERD, fatness, and tobacco ingesting. Broadcast for EC will possible play an indispensable function in preventative, therefore, mortality in the future (Uhlenhopp, Then, Sunkara, & Gaduputi, 2020) [68]. Additional study presented numerous risk influences for ESCC are outstanding to a union of factors, as well as current damage, revelation to polycyclic aromatic hydrocarbons (from opium and interior

air contamination), and nutrient-deficient regimes. Furthermore related risk of ESCC with experience to uniped water and tooth injury (Sheikh *et al*., 2019) [58].

Markers of EC

Cancer markers of this malignancy are an proceeding range of enquiry that can possibly perform to prior analysis along with singing a portion in evaluating cancer retort to treatment (Napier *et al*., 2014) [43]. Identification of markers related through gastric region CSCs, such as CD44, CD133, ALDH1, CD24, and BMI1, has complete it conceivable to advance more correct finding attitudes. (Rassouli *et al*., 2016) [53]. Unlike indicators and paths, for example CD44/CD24, CD133, Notch, and Wnt/β-catenin, are relaxed in precise cancer suitcases, even in EC. As a result, their function must be understood in order for these indicators and trails to be targeted to plan conclusive healing methods in opposition to drug-resistant EC and to resolve the challenge of growth decrease (Qian *et al*., 2016) [52].

In (ESCC), there are numerous symbols such as ALDH, Pygo2, MAML1, Twist1, Musashi1, Side population (SP), CD271 and CD90 that have been projected to recognize the CSCS in distinct cancer commonalities. In ESCC, (p75NTR) is uttered in a contender CSC populace viewing great tumorigenicity and chemo-resistance (Kojima *et al*., 2017) [27]. ESCC patients with a high CD133-CXCR4 appearance may be a good candidate for early detection, and CD133 and CXCR4 may be useful in identifying individuals who may benefit from further investigation (Lu *et al*., 2015).

Cancer stem cell in GI

Cancers are collected of diverse sorts of cancer cells that donate to growth heterogeneity. Amongst these populaces of cells, Cancer stem cells (CSCs) show a significant character in malignance beginning and evolution (Papaccio *et al*., 2017) [49]. Cells of the immune system called CSCs are minor occupants of cancer cells that have the ability to self-renew and discriminate, as well as tumorigenicity, metastasis, and chemo-resistant properties (Okumura, Kojima, Yamaguchi, & Shimada, 2018) [46].

These clles are normally accountable for cancer origination and poor prediction (L Vermeulen, Sprick, Kemper, Stassi, & Medema, 2008) [71] they were principal recognized in hematological distortions, mostly in severe myelogenous leukemia (Bonnet & Dick, 1997) [7]. Formerly CSCs were create in dense tumors (Moore & Lemischka, 2006) [40]. In most cases, xenotransplantation of prospectively separated cells contributes significantly to human CSCs' existence; yet, their clonal dynamics and adaptability are still poorly understood (Shimokawa *et al*., 2017) [59]. Throughout the previous decade, a stem-cell-like subsection of malignance cells has been recognized in several distortions (Louis Vermeulen, e Melo, Richel, & Medema, 2012) [70]. These kind of cells, denoted to as CSCs which are the key funders to chemo-resistance, and are accountable for tumor development and reappearance after conservative therapy (Saikawa *et al*., 2010) [56]. The population cells are branded by their aptitude to generate tumor cells with dissimilar phenotypes (Adams & Strasser, 2008) [2]. Chemo-resistance and metastasis in EC are mostly attributed to the presence of stem cell-like side populaces (Y. Zhao *et al*., 2014) [80].

Colony construction, relocation and drug struggle capacities were melodramatically reserved in ESCC cells. SP cells and sphere development cells might be respectable replicas for CSCs in ESCC cell lines (Teng *et al*., 2018) [64]. It has moreover been established that stalk cell markers similar ALDH1, HIWI, Oct3/4, ABCG2, SOX2, SALL4, BMI-1, NANOG, CD133 and podoplanin are allied with patient's projection, uncontrolled steps, cancer return and treatment confrontation (Islam, Gopalan, Wahab, Smith, & Lam, 2015) [22].

Inactive CSCs have developed tumorigenicity and chemo-resistance than other CSCs, representative that they are further accountable for the malevolent potential of cancers and they can be rather actual healing boards (L. Li & Bhatia, 2011) [29].

CD133 gene

CD133 is unique of the signs that is recycled for the documentation of CSC (Anbarlou *et al*., 2015) [3]. Prominin, a pent span membrane glycoprotein, was initially identified in 1997 in two sovereign institutions of higher learning. CD133, previously known as PROML-1 or AC133, was first discovered as a homolog of mouse prominin, a pentaspan transmembrane glycoprotein found in the plasma membrane protrusions of murine neuroepithelial stem cells. CD133 is a transmembrane glycoprotein found in the plasma membrane protrusions of neuroepithelial stem cells (Fargeas, Corbeil, & Huttner, 2003) [14]. Human CD133 (Thamm, Graupner, Werner, Huttner, & Corbeil, 2016) [65] is an 865 amino acid protein, which covers 5 transmembrane domains and 2 large glycosylated extracellular rings. The foretold size of CD133 is 97 kDa, but the real molecular weight of glycosylated CD133 is 120 kDa (Miraglia *et al*., 1997) [37]. Glycosylation of CD133 harvests a 120 kDa protein and changes the general tertiary construction and constancy of CD133 (Elsaba *et al*., 2010 [11]; Thamm *et al*., 2016) [65]. PROM1 gene encrypts CD133 protein, which is a cell superficial marker of hematopoietic SCs, prostatic epithelial SCs, pancreatic SCs, leukemic SCs, liver CSCs, and CRC stem cells (P. Zhao, Li, & Lu, 2010) [79].

Many diverse molecular instruments have been examined to improved comprehend the cadence of CD133 in normal and CSCs. Researchers working with both normal and CSC cell lines have determined that CD133 antibody reactivity is reduced when cells are in the G1/G0 phase of the cell cycle, as opposed to the G2/M phase of the cell cycle, indicating that CD133 expression is associated with a specific level of cell cycle requirement (Jaksch, Múnera, Bajpai, Terskikh, & Oshima, 2008) [23]. The biological role of the CD133 molecule is unidentified (Brossa *et al*., 2018) [8].

Higher CD133 expression is meaningfully related with lymph node metastasis, aloof metastasis, clinical stage and histopathological score (Sui *et al*., 2016) [63] (G.-H. Zhao & Yu, 2017) [78]. Following the training, it was discovered that CD133 immunoreactivity is a reliable predictor of prognosis in ESCC patients. Additionally, CD133 may have a function in the control of the tumor cell cycle in ESCC through the expression of p27 and p16. As a result, it is still debated whether CD133 expression is a legitimate prognostic diagnostic for ESCC at the present time (Okamoto *et al*., 2013) [45].

Grounded on the outcomes of other study, they decided that CD133 is an effectual prognostic factor in esophageal carcinoma (Sui *et al*., 2016) [63] CD133 expression by immunohistochemical staining in patients with ESCC (n = 86)

and renowned that cytoplasmic expression of CD133 was meaningfully connected with overall survival of patients with ESCC (Okamoto *et al*., 2013) [45]. It is widely believed that tumors are initiated and maintained by a small population of cancer cells known as tumor-initiating cells (TICs), which have the unique ability to reintroduce themselves incessantly and to resist conventional therapy. CD133 is one of the most commonly used markers for classifying TICs, and it is one of the most commonly used markers for classifying TICs (Valent *et al*., 2012) [69]. CD133 was described to be a TIC marker in numerous cancer categories (Hang *et al*., 2012) [20].

Observations concerning a nonexistence of prominin-1 causes a fault in external part morphogenesis that can lead to sightlessness (Goldberg, Moritz, & Williams, 2016) [18]. Even though AC133 mRNA is noticed in dissimilar tissues, its expression in the hematopoietic system is controlled to $CD34^{+}$stem cells. AC133 is likewise expressed on stem cells of other tissues, counting endothelial progenitor cells.

Positivity for the external proteins CD133 has been hired in various trainings to separate cells with stem cell-like and cancer-initiating possessions from diverse solid tumors. Additionally, its prognostic and clinicopathological morals in unlike cancer types have been broadly studied (Long *et al*., 2015) [33].

CD133 has been assumed to recognize CSC populaces in numerous solid tumor kinds counting some forms of brain cancer (Long *et al*., 2015) [33] prostate cancer (Glumac *et al*., 2018) [16, 17] colon cancer (O'Brien, Pollett, Gallinger, & Dick, 2007) [44] lung cancer (Esheba, Hassan, El Bostany, & Aly, 2017) [12] hepatocellular carcinoma (Won *et al*., 2015) [74] and ovarian cancer (Zhou *et al*., 2015) [81].

Conclusion

Depending on the consequences of this education, we accomplish that CD133 attends as a prognostic indicator of poor prediction. Complex CD133 appearance is meaningfully related by way of lymph bulge metastasis, unfriendly metastasis and progressive scientific phase. This marker has been recommended to mark CSC in numerous tumor sorts, though, the accurateness of CD133 as a CSC biomarker has been extremely contentious. Furthermore, it might signify valuable extrapolative marker in patients exaggerated by esophageal cancer. This research demonstrated that CD133 immuno reactivity is a reasonable predictor of prognosis in individuals with end-stage renal cancer (ESCC). In all, CD133 has the potential to play a role in the direction of growing cell series in ESCC, according to the researchers. At current, it therefore remnants provocative whether CD133 appearance is an effective analytical indicator for ESCC. To explain this connection, additional inquiries are obligatory.

References

1. Abbas G, Krasna M. Overview of esophageal cancer. Annals of cardiothoracic surgery. 2017;6(2):131.
2. Adams JM, Strasser A. Is tumor growth sustained by rare cancer stem cells or dominant clones? Cancer research. 2008;68(11):4018-4021.
3. Anbarlou A, Atashi A, Soleimani M, Akhavan Rahnama M, Bohloli M, Mossahebi-Mohammadi M *et al*. Differential characteristics of CD133+ and CD133- Jurkat cells. In Vitro Cellular & Developmental Biology-Animal. 2015;51(6):556-561.
4. Arnold M, Laversanne M, Brown LM, Devesa SS, Bray F. Predicting the future burden of esophageal cancer by histological subtype: international trends in incidence up to 2030. Official journal of the American College of Gastroenterology| ACG. 2017;112(8):1247-1255.
5. Arnold M, Soerjomataram I, Ferlay J, Forman D. Global incidence of oesophageal cancer by histological subtype in 2012. Gut. 2015;64(3):381-387.
6. Bishak YK, Payahoo L, Osatdrahimi A, Nourazarian A. Mechanisms of cadmium carcinogenicity in the gastrointestinal tract. Asian Pacific Journal of Cancer Prevention. 2015;16(1):9-21.
7. Bonnet D, Dick JE. Human acute myeloid leukemia is organized as a hierarchy that originates from a primitive hematopoietic cell. Nature medicine. 1997;3(7):730-737.
8. Brossa A, Papadimitriou E, Collino F, Incarnato D, Oliviero S, Camussi G *et al*. Role of CD133 molecule in Wnt response and renal repair. Stem cells translational medicine. 2018;7(3):283-294.
9. Colquhoun A, Arnold M, Ferlay J, Goodman K, Forman, D, Soerjomataram I *et al*. Global patterns of cardia and non-cardia gastric cancer incidence in 2012. Gut. 2015;64(12):1881-1888.
10. Dulak AM, Stojanov P, Peng S, Lawrence MS, Fox C, Stewart C *et al*. Exome and whole-genome sequencing of esophageal adenocarcinoma identifies recurrent driver events and mutational complexity. Nature genetics. 2013;45(5):478-486.
11. Elsaba TM, Martinez-Pomares L, Robins AR, Crook S, Seth R, Jackson D *et al*. The stem cell marker CD133 associates with enhanced colony formation and cell motility in colorectal cancer. PLoS One. 2010;5(5):e10714.
12. Esheba GE, Hassan AA, El Bostany MZ, Aly MH. Prognostic value of cancer stem cell markers and E-cadherin expression in non-small-cell lung cancer. Egyptian Journal of Pathology. 2017;37(2):281-288.
13. Fargeas CA, Büttner E, Corbeil D. Commentary: "prom1 function in development, intestinal inflammation, and intestinal tumorigenesis". Frontiers in oncology. 2015; 5:91.
14. Fargeas CA, Corbeil D, Huttner WB. AC133 antigen, CD133, prominin-1, prominin-2, etc.: prominin family gene products in need of a rational nomenclature. Stem cells. 2003;21(4):506-508.
15. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM *et al*. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. International journal of cancer. 2010;127(12):2893-2917.
16. Glumac PM, Forster CL, Zhou H, Murugan P, Gupta S, LeBeau AM *et al*. The identification of a novel antibody for CD133 using human antibody phage display. The Prostate. 2018;78(13):981-991.
17. Glumac PM, LeBeau AM. The role of CD133 in cancer: a concise review. Clinical and translational medicine. 2018;7(1):1-14.
18. Goldberg AF, Moritz OL, Williams DS. Molecular basis for photoreceptor outer segment architecture. Progress in retinal and eye research. 2016;55:52-81.
19. Gupta V, Bhardwaj S, Bhagat OK. Pattern of esophageal cancer in tertiary care hospital in North India: a clinicopathological study. International Journal of Research in Medical Sciences. 2017;5(4):1405-1409.
20. Hang D, Dong HC, Ning T, Dong B, Hou DL, Xu WG *et*

al. Prognostic value of the stem cell markers CD133 and ABCG2 expression in esophageal squamous cell carcinoma. Diseases of the Esophagus. 2012;25(7):638-644.
21. Huang FL, Yu SJ. Esophageal cancer: risk factors, genetic association, and treatment. Asian journal of surgery. 2018;41(3):210-215.
22. Islam F, Gopalan V, Wahab R, Smith RA, Lam AKY. Cancer stem cells in oesophageal squamous cell carcinoma: Identification, prognostic and treatment perspectives. Critical reviews in oncology/hematology. 2015;96(1):9-19.
23. Jaksch M, Múnera J, Bajpai R, Terskikh A, Oshima RG. Cell cycle–dependent variation of a CD133 epitope in human embryonic stem cell, colon cancer, and melanoma cell lines. Cancer research. 2008;68(19):7882-7886.
24. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun M. Cancer statistics. CA Cancer J Clin., 2009, 59(4).
25. Katoh Y, Katoh M. Comparative genomics on PROM1 gene encoding stem cell marker CD133. International journal of molecular medicine. 2007;19(6):967-970.
26. Khorshidi H, Taghipour M, Yousefi B, Dehghan A. Esophageal Squamous Cell Carcinoma Presenting as Two Simultaneous Adjacent Masses Confirmed by Pathologic Findings: Report of a Rare Case. Case Reports in Clinical Practice. 2018;3(1):21-25.
27. Kojima H, Okumura T, Yamaguchi T, Miwa T, Shimada Y, Nagata T *et al*. Enhanced cancer stem cell properties of a mitotically quiescent subpopulation of p75NTR-positive cells in esophageal squamous cell carcinoma. International Journal of Oncology. 2017;51(1):49-62.
28. Li B, Xu W, Han L, Chan K, Tsao S, Lee N *et al*. MicroRNA-377 suppresses initiation and progression of esophageal cancer by inhibiting CD133 and VEGF. Oncogene. 2017;36(28):3986-4000.
29. Li L, Bhatia R. Stem cell quiescence. Clinical cancer research. 2011;17(15):4936-4941.
30. Li XM, Wang H, Zhu LL, Zhao RZ, Ji HL. Genes regulating epithelial polarity are critical suppressors of esophageal oncogenesis. Journal of Cancer. 2015;6(8):694.
31. Liu R, Li X, Hylemon PB, Zhou H. Conjugated bile acids promote invasive growth of esophageal adenocarcinoma cells and cancer stem cell expansion via sphingosine 1-phosphate receptor 2–mediated Yes-associated protein activation. The American journal of pathology. 2018;188(9):2042-2058.
32. Liu Y, Ren S, Xie L, Cui C, Xing Y, Liu C *et al*. Mutation of N-linked glycosylation at Asn548 in CD133 decreases its ability to promote hepatoma cell growth. Oncotarget. 2015;6(24):20650.
33. Long H, Xiang T, Qi W, Huang J, Chen J, He L *et al*. CD133+ ovarian cancer stem-like cells promote non-stem cancer cell metastasis via CCL5 induced epithelial-mesenchymal transition. Oncotarget. 2015;6(8):5846.
34. Lu C, Xu F, Gu J, Yuan Y, Zhao G, Yu X *et al*. Clinical and biological significance of stem-like CD133+ CXCR4+ cells in esophageal squamous cell carcinoma. The Journal of thoracic and cardiovascular surgery. 2015;150(2):386-395.
35. Markar SR, Arhi C, Leusink A, Vidal-Diez A, Karthikesalingam A, Darzi A *et al*. The influence of antireflux surgery on esophageal cancer risk in England: national population-based cohort study. Annals of surgery. 2018;268(5):861-867.
36. Mima K, Ogino S, Nakagawa S, Sawayama H, Kinoshita K, Krashima R *et al*. The role of intestinal bacteria in the development and progression of gastrointestinal tract neoplasms. Surgical oncology. 2017;26(4):368-376.
37. Miraglia S, Godfrey W, Yin AH, Atkins K, Warnke R, Holden JT *et al*. A novel five-transmembrane hematopoietic stem cell antigen: isolation, characterization, and molecular cloning. Blood, The Journal of the American Society of Hematology. 1997;90(12):5013-5021.
38. Moghbeli M, Moghbeli F, Forghanifard MM, Abbaszadegan MR. Cancer stem cell detection and isolation. Medical Oncology. 2014;31(9):69.
39. Mohamad Amin P, Mohsen V, Ahmad Reza B. Burden of gastrointestinal cancer in Asia; an overview, 2015.
40. Moore KA, Lemischka IR. Stem cells and their niches. Science. 2006;311(5769):1880-1885.
41. Nakashima Y, Saeki H, Hu Q, Tsuda Y, Hisamatsu Y, Ando K *et al*. Neoadjuvant chemotherapy versus chemoradiotherapy for patients with esophageal squamous cell carcinoma. Anticancer research. 2018;38(12):6809-6814.
42. Nakashima Y, Saeki H, Yukaya T, Tsutsumi S, Nakanishi R, Sugiyama M *et al*. Blood flow assessment with indocyanine green fluorescence angiography for pedicled omental flap on cervical esophagogastric anastomosis after esophagectomy. Journal of the American College of Surgeons. 2016;222(5):e67-e69.
43. Napier KJ, Scheerer M, Misra S. Esophageal cancer: A Review of epidemiology, pathogenesis, staging workup and treatment modalities. World journal of gastrointestinal oncology. 2014;6(5):112.
44. O'Brien CA, Pollett A, Gallinger S, Dick JE. A human colon cancer cell capable of initiating tumour growth in immunodeficient mice. Nature. 2007;445(7123):106-110.
45. Okamoto H, Fujishima F, Nakamura Y, Zuguchi M, Ozawa Y, Takahashi Y *et al*. Significance of CD133 expression in esophageal squamous cell carcinoma. World journal of surgical oncology. 2013;11(1):1-9.
46. Okumura T, Kojima H, Yamaguchi T, Shimada Y. Clinical application of stem cell biology in esophageal cancer. In Molecular Diagnosis and Targeting for Thoracic and Gastrointestinal Malignancy: Springer, 2018, 49-62.
47. Oteiza P, Fraga CG, Mills D, Taft D. Flavonoids and the gastrointestinal tract: Local and systemic effects. Molecular aspects of medicine. 2018;61:41-49.
48. Sukmawati Tansil Tan, Yohanes Firmansyah, Jessica Elizabeth. New approach to skin burn treatment: Potential of Secretome from Wharton's jelly Mesenchymal stem cell therapy. Int. J Adv. Biochem. Res. 2020;4(2):11-16. DOI: 10.33545/26174693.2020.v4.i2a.49
49. Papaccio F, Paino F, Regad T, Papaccio G, Desiderio V, Tirino V *et al*. Concise review: cancer cells, cancer stem cells, and mesenchymal stem cells: influence in cancer development. Stem cells translational medicine. 2017;6(12):2115-2125.
50. Peichev M, Naiyer AJ, Pereira D, Zhu Z, Lane WJ, Williams M *et al*. Expression of VEGFR-2 and AC133 by circulating human CD34+ cells identifies a population of functional endothelial precursors. Blood, The Journal of the American Society of Hematology. 2000;95(3):952-958.
51. Pennathur A, Gibson MK, Jobe BA, Luketich JD. Oesophageal carcinoma. THE LANCET.

2013;81(9864):400-412.
52. Qian X, Tan C, Wang F, Yang B, Ge Y, Guan Z *et al*. Esophageal cancer stem cells and implications for future therapeutics. OncoTargets and therapy. 2016;9:2247.
53. Rassouli FB, Matin MM, Saeinasab M. Cancer stem cells in human digestive tract malignancies. Tumor Biology. 2016;37(1):7-21.
54. Rozen P. Cancer of the gastrointestinal tract: early detection or early prevention? European Journal of Cancer Prevention. 2004;13(1):71-75.
55. Saeki H, Nakashima Y, Hirose K, Sasaki S, Jogo T, Taniguchi D *et al*. Energy-less technique with mini-clips for recurrent laryngeal nerve lymph node dissection in prone thoracoscopic esophagectomy for esophageal cancer. The American Journal of Surgery. 2018;216(6):1212-1214.
56. Saikawa Y, Fukuda K, Takahashi T, Nakamura R, Takeuchi H, Kitagawa Y *et al*. Gastric carcinogenesis and the cancer stem cell hypothesis. Gastric Cancer. 2010;13(1):11-24.
57. Sardana RK, Chhikara N, Tanwar B, Panghal A. Dietary impact on esophageal cancer in humans: a review. Food & function. 2018;9(4):1967-1977.
58. Sheikh M, Poustchi H, Pourshams A, Etemadi A, Islami F, Khoshnia M *et al*. Individual and combined effects of environmental risk factors for esophageal cancer based on results from the Golestan Cohort Study. Gastroenterology. 2019;156(5):1416-1427.
59. Shimokawa M, Ohta Y, Nishikori S, Matano M, Takano A, Fujii M *et al*. Visualization and targeting of LGR5+ human colon cancer stem cells. Nature. 2017;545(7653):187-192.
60. Shmelkov SV, Jun L, St Clair R, McGarrigle D, Derderian CA, Usenko JK *et al*. Alternative promoters regulate transcription of the gene that encodes stem cell surface protein AC133. Blood. 2004;103(6):2055-2061.
61. Shmelkov SV, Meeus S, Moussazadeh N, Kermani P, Rashbaum WK, Rabbany SY *et al*. Cytokine preconditioning promotes codifferentiation of human fetal liver CD133+ stem cells into angiomyogenic tissue. Circulation. 2005;111(9):1175-1183.
62. Song M, Garrett WS, Chan AT. Nutrients, foods, and colorectal cancer prevention. Gastroenterology. 2015;148(6):1244-1260.e1216.
63. Sui YP, Jian XP, Ma L, Xu GZ, Liao HW, Liu YP *et al*. Prognostic value of cancer stem cell marker CD133 expression in esophageal carcinoma: A meta-analysis. Molecular and clinical oncology. 2016;4(1):77-82.
64. Teng Y, Yu X, Yuan H, Guo L, Jiang W, Lu SH *et al*. DNMT1 ablation suppresses tumorigenesis by inhibiting the self-renewal of esophageal cancer stem cells. Oncotarget. 2018;9(27):18896.
65. Thamm K, Graupner S, Werner C, Huttner WB, Corbeil D. Monoclonal antibodies 13A4 and AC133 do not recognize the canine ortholog of mouse and human stem cell antigen prominin-1 (CD133). PLoS One. 2016;11(10):e0164079.
66. Thrift AP. The epidemic of oesophageal carcinoma: where are we now? Cancer epidemiology. 2016;41:88-95.
67. Torre LA, Siegel RL, Ward EM, Jemal A. Global cancer incidence and mortality rates and trends an update. Cancer Epidemiology and Prevention Biomarkers. 2016;25(1):16-27.
68. Uhlenhopp DJ, Then EO, Sunkara T, Gaduputi V. Epidemiology of esophageal cancer: update in global trends, etiology and risk factors. Clinical journal of gastroenterology, 2020, 1-12.
69. Valent P, Bonnet D, De Maria R, Lapidot T, Copland M, Melo JV *et al*. Cancer stem cell definitions and terminology: the devil is in the details. Nature reviews cancer. 2012;12(11):767-775.
70. Vermeulen L, e Melo FdS, Richel DJ, Medema JP. The developing cancer stem-cell model: clinical challenges and opportunities. The lancet oncology. 2012;13(2):e83-e89.
71. Vermeulen L, Sprick M, Kemper K, Stassi G, Medema J. Cancer stem cells–old concepts, new insights. Cell Death & Differentiation. 2008;15(6):947-958.
72. Wang D, Plukker JTM, Coppes R. Cancer stem cells with increased metastatic potential as a therapeutic target for esophageal cancer. Paper presented at the Seminars in cancer biology, 2017.
73. Weigmann A, Corbeil D, Hellwig A, Huttner WB. Prominin, a novel microvilli-specific polytopic membrane protein of the apical surface of epithelial cells, is targeted to plasmalemmal protrusions of non-epithelial cells. Proceedings of the National Academy of Sciences. 1997;94(23):12425-12430.
74. Won C, Kim BH, Yi EH, Choi KJ, Kim EK, Jeong JM *et al*. Signal transducer and activator of transcription 3-mediated CD133 up-regulation contributes to promotion of hepatocellular carcinoma. Hepatology. 2015;62(4):1160-1173.
75. Wu IC, Syu HY, Jen CP, Lu MY, Chen YT, Wu MT, Wang HC *et al*. Early identification of esophageal squamous neoplasm by hyperspectral endoscopic imaging. Scientific reports. 2018;8(1):1-10.
76. Xu Y, Yu X, Chen Q, Mao W. Neoadjuvant versus adjuvant treatment: which one is better for resectable esophageal squamous cell carcinoma? World journal of surgical oncology. 2012;10(1):1-8.
77. Zhang Y. Epidemiology of esophageal cancer. World journal of gastroenterology: WJG. 2013;19(34):5598.
78. Zhao GH, Yu T. Clinicopathological and prognostic significance of cd133 in esophageal cancer: a meta-analysis. International journal of clinical and experimental medicine. 2017;10(1):115-+.
79. Zhao P, Li Y, Lu Y. Aberrant expression of CD133 protein correlates with Ki-67 expression and is a prognostic marker in gastric adenocarcinoma. BMC cancer. 2010;10(1):1-6.
80. Zhao Y, Bao Q, Schwarz B, Zhao L, Mysliwietz J, Ellwart J, Camaj P *et al*. Stem cell-like side populations in esophageal cancer: a source of chemotherapy resistance and metastases. Stem cells and development. 2014;23(2):180-192.
81. Zhou Q, Chen A, Song H, Tao J, Yang H, Zuo M *et al*. Prognostic value of cancer stem cell marker CD133 in ovarian cancer: a meta-analysis. International journal of clinical and experimental medicine. 2015;8(3):3080.
82. Pakzad R, Mohammadian-Hafshejani A, Khosravi B, Soltani S, Pakzad I, Mohammadian M *et al*. The incidence and mortality of esophageal cancer and their relationship to development in Asia. Annals of translational medicine, 2016, 4(2).