Why Interleukin-17A is the most Potential Next Generation Drug Target in Angiogenesis-mediated diseases

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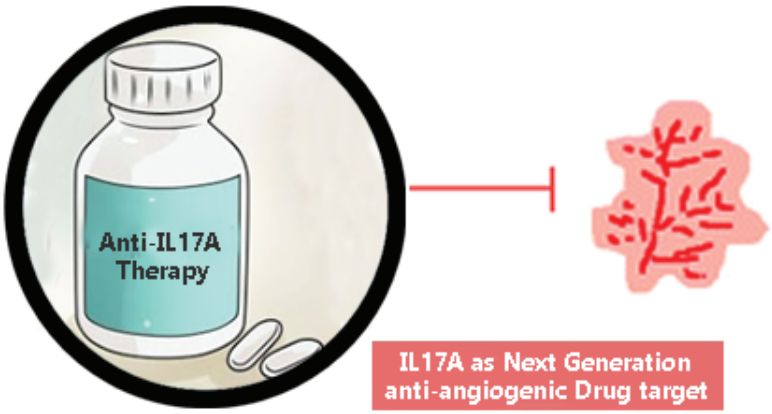
Graphical Abstract



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Cancer treatment is investigated worldwide using various resources. The molecular pathogenesis of cancer gives us advantages to find potential anticancer drugs. Scientists are now more prone to develop drugs that bind in a specific site to decrease the potential side effects and prolong the cure. The treatment of cancer can be divided into different categories. Surgery is the first line treatment for solid tumors and the early stages of cancer. Even benign growths can be removed by this technique (Abeloff , 2008; Edmund et al., 2007). The goal of radiation treatment is the direct killing of cancerous cells. Chemotherapy is the most widely used drug for cancer treatment and prevention but it is not widely accepted for its chronic side effect. Hormonal drugs are designed to prevent the signaling process for continued growth and division of cells that are hormone dependent. Antibodies work as specific inhibitors either depriving the signal for cancer cells or inducing cell death. Complementary and alternative medicines are used to slow down the cancer progress. Vaccines, biological response modifiers and targeted therapies are very recent inclusions in the fight against cancer. From these vast treatment sciences, only molecular targeted drug could be the next generation anticancer therapy. Molecular scientists are searching for the crucial biological factors that cause tumor development and subsequent metastatic phase. Recently, it was found that Interleukin-17 has an association to human malignancy (Tartour et al., 1999; Numasaki et al., 2003; Kato et al., 2001). IL-17 is the core factor to promote tumor development, tumor growth and angiogenesis. Thus, this molecular targeted drug can be investigated to cure cancer. Ligand mediated drugs can be designed to target this IL-17 protein with very few side effect.

Significance | Despite the use of IL17A in the rheumatoid arthritis, it is not used as therapeutic target in cancer. Targeting IL17A can control the hundreds of the bio-markers in cancer.

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Potential next generation drug target in cancer

A pro-inflammatory cytokine is produced by activated CD4+ memory T cells in carcinogenesis to generate interleukin-17 A (IL-17A). IL-17A induces neoplastic transformation of JB6 Cl41 cells through activation of the tumor progression locus 2 (TPL2). IL-17A dose- and time-dependently increases TPL2 phosphorylation in JB6 Cl41 cells through the IL-17A receptor. IL-17A activates mitogen-activated protein kinase/extracellular signal-regulated kinase kinases, c-jun N-terminal kinases and STAT3 signaling pathways, which are inhibited by a TPL2 kinase inhibitor (TKI). Furthermore, IL-17A activates c-fos and c-jun promoter activity, resulting in increased activator protein-1 (AP-1) activity. When small interfering RNA against IL-17A receptor (IL-17R), IL-17A and TPL2 were introduced into JB6 Cl41 cells, IL-17A-induced AP-1 activity was significantly decreased compared with control cells. Similarly, TPL2 inhibition suppressed AP-1 activity induced by IL-17A. The knockdown of IL-17R and TKI in JB6 Cl41 cells resulted in decreased IL-17A-induced cell transformation. IL-17A-induced TPL2 signaling pathway supports the notion of cancer-associated inflammation in the tumor micro-environment. Therapeutic approaches that target this pathway may effectively inhibit carcinogenesis (Garam et al., 2012). IL-17-induced MMPs have a role in PIN-to-cancer transition. IL-17 promotes prostate cancer formation and growth via induction of MMP expression (Zhang et al., 2014). Pro-inflamma-

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tory cytokines have an important anti-tumorigenic role and in the growth and spread of the malignancy (Coussens and Werb, 2002; Wilson and Balkwill, 2002). Furthermore, Interleukin-1 (IL-1) and IL-6 induce proliferation and prolonged cell survival (Miki et al., 2002; Lus and Donovan, 1999; Ito and and Miki, 1999).

The pro-inflammatory cytokine IL-17 is produced by activated CD4 T-cells and CD8 T-cells (in human) (Yao et al., 1995; Shin et al., 1999). IL-17 and and IL-6 promote the tumourigenicity of human cervical cancer, ovarian cancers and promotes tumour angiogenesis due to the enhancement of vascular endothelial growth factor (VEGF) (Tartour et al., 1999; Pages et al., 1999; Kato et al., 2001; Numasaki et al., 2003; Takahashi et al., 2005; Wong et al., 1999). There is a correlation between vascularity and invasive behaviour in CRC (Choi et al., 1998). IL-1, and IL-6 have been associated with colorectal cancer (Komoda et al., 1998). IL-17 induces IL-1 from macrophages to stimulate epithelial and fibroblastic cells to secrete IL-6(Jovanovic et al., 1998; Fossiez et al., 1996). IL-17 is demonstrated to increase the production of active metalloproteinase MMP-9 (Prause et al., 2004). The role of metalloproteinases in the progression of human malignancies is well documented in numerous reports (Matrisian et al., 1994; Roeb et al., 2001). [To be continued...]

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Md Shamsuddin S. K. made substantial contributions to the conception of the editorial topics.

Competing financial interests

The editor(s) declare no competing financial interests.

References

Abeloff, Martin D. (2008). Abeloff's Clinical Oncology.4th ed. Philadelphia: Churchill Livingstone.

Banchereau J and Lebecque S. T. (1996). cell interleukin-17 induces stromal cells to produce proinflammatory and hematopoietic cytokines. J. Exp. Med., 183, 2411-2415.

Coussens LM and Werb Z. (2002). Inflammation and cancer. Nature 420, 860-867.

Choi HJ, Hyun MS, Jung GJ, Kim SS and Hong SH. (1998). Tumor angiogenesis as a prognostic predictor in colorectal carcinoma with special reference to mode of metastasis and recurrence. Oncology, 55, 575-581.

Edmund H. Duthie Jr., Paual R. Katz, Michael L. Malone. (2007). Practice of Geriatrics. 4th ed. Philadelphia: Saunders.

Fossiez F, Djossou O, Chomarat P, Flores-Romo L, Ait-Yahia S, Maat C et al. (1994). Matrixdegrading metalloproteinases in tumor progression. Princess Takamatsu Symp., 24, 152-161

Fridman S. (1999). Interleukin-17 a T-cell mediated cytokine promotes tumorigenicity of human cervical tumors in nude mice. Cancer Res., 59, 3698-3704

Garam Kim, Prem Khanal, Sung-Chul Lim, Hyo Jeong Yun, Sang-Gun Ahn, Sung Hwan Ki and Hong Seok Choi. (2012). Interleukin-17 induces AP-1 activity and cellular transformation via upregulation of tumor progression locus 2 activity, Carcinogenesis

Ito H. and Miki C. (1999). Profile of circulating levels of interleukin-1 receptor antagonist and interleukin-6 in colorectal cancer patients. Scand J Gastroenterol 11, 1139-1143.

Jovanovic DV, Di Battista JA, Martel-Pelletier J, Jolicoeur FC, He Y, Zhang M, Mineau F and Pelletier JP. (1998). IL-17 stimulates the production and expression of proinflammatory cytokines, IL-1beta and TNF-alpha by human macrophages. J. Immunol. 160, 3513-3521.

Kato T, Furumoto H, Ogura T, Onishi Y, Irahara M, Yamano S, Kamada M, Aono T (2001). Expression of IL-17 mRNA in ovarian cancer. Conference abstract.

Kato T, Furumoto H, Ogura T, Onishi Y, Irahara M, Yamano S, Kamada M and Aono T. (2001). Expressiom of IL-17 mRNA in Ovarian Cancer. Biochem. Biophys. Res. Commun. 282, 735-738

Komoda H, Tanaka M, Matsuo Y, Hazama K and Takao T. (1998). Interleukin 6 levels in colorectal cancer tissues. World J. Surg. 22, 895-898.

Lust JA and Donovan KA. (1999). The role of interleukin-1, in the pathogenesis of multiple myeloma. Hematol Oncol Clin North Am 13, 1117-1125.

Miki C, Tonouchi H, Wakuda R, Hatada T, Inoue Y, Minato E, Kobayashi M and Kusunoki M. (2002). Intra-tumoral interleukin-6 downregulation system and genetic mutations of tumor suppressor genes in colorectal cancer. Cancer 94, 1584-1592.

Numasaki M, Fukushi J, Ono M, Narula SK, Zavodny PJ, Kudo T, Robbins PD, Tahara H, Lotze MT. (2003). Interleukin-17 promotes angiogenesisand tumor growth. Blood 101, 2620-2627.

Pages F, Vives V, Sautes-Fridman C, Fossiez F, Berger A, Cugnenc PH, Tartour E and Fridman WH. (1999). Control of tumor development by intratumoral cytokines. Immunol. Lett. 68, 135-139.

Prause O, Bozinovski S, Anderson GP and Linden A. (2004). Increased matrix metalloproteinase-9 concentration and activity after stimulation with interleukin-17 in mouse airways. Thorax 59, 313-317.

Roeb E, Dietrich CG, Winograd R, Arndt M, Breuer B, Fass J, Scumpelick V and Matern S. (2001). Activity and cellular origin of gelatinases in patients with colon and rectal cancer differential activity of matrix metalloproteinase-2. Cancer 92, 2680-2691.

Shin HC, Benbernou N, Esnault S and Guenounou M. (1999). Expression of IL-17 in human memory CD45RO+ T lymphocytes and its regulation by protein kinase A pathway. Cytokine 11, 257-266.

Tartour E, Fossiez F, Joyeux I, Galinha A, Gey A, Claret E, Sastre- Garau X, Couturier J, Mosseri V, Vives V, Banchereau J, Fridman WH, Wijdenes J, Lebecque S, Sautès-Fridman C. (1999). Interleukin 17, a T-cell-derived cytokine, promotes tumorigenicity of human cervical tumors in nude mice. Cancer Res. 59, 3698-3704.

Takahashi H, Numasaki M, Lotze MT and Sasaki H. (2005). Interleukin-17 enhances bFGF, HGF and VEGF-induced growth of vascular endothelial cells. Immunol. Lett. 98, 189-193.

Wilson J. and Balkwill F. (2002). The role of cytokines in the epithelial cancer microenvironment. Semin Cancer Biol 12, 113-120.

Wong MP, Cheung N, Yuen ST, Leung SY and Chung LP. (1999). Vascular endothelial growth factor is up-regulated in the early premalignant stage of colorectal tumour progression. Int. J. Cancer 81, 845-850.

Yao Z, Franslow WC, Seldin MF, Rousseau A-M, Painter SL, Comeau MR, Cohen JI and

Spriggs MK. (1995). Herpesvirus saimiri encodes a new cytokine IL-17 which binds to novel cytokine receptor. Immunity 3, 811-821.

Zhang QY, Liu S, Ge D, Li C, Xue Y, Zhang QS, and You Z. The role of interleukin-17 in formation and growth of prostate cancer, Tulane University School of Medicine, Cancer research abstract.