EBioMedicine 26 (2017) 10

Contents lists available at ScienceDirect

EBioMedicine

journal homepage: www.ebiomedicine.com

Commentary

Deguelin, a Novel Anti-Tumorigenic Agent in Human Esophageal Squamous Cell Carcinoma

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ARTICLE INFO

Article history:
Received 15 November 2017
Accepted 15 November 2017
Available online 16 November 2017

Keywords:
Deguelin
Anti-tumorigenic agent
Esophageal squamous cell carcinoma

Deguelin is a natural rotenoid extracted from several plants, including *Derris trifoliate* (Lour.) or *Mundulea sericea* (Leguminosae). It has been considered as an anti-tumor agent targeting apoptosis, cell cycle arrest and anti-angiogenesis for cancer chemoprevention (Wang et al., 2013). Recent reports have described multiple molecular mechanisms of deguelin function. Deguelin arrests the cell-cycle at G_2-M phase in Raji cells derived from B lymphoblast of Burkitt's lymphoma patient (Xiong and Liu, 2013). Interestingly, deguelin-induced cell cycle arrest seems to vary in various cancer cell lines even same origin of disease, because deguelin function has been known as G_0-G_1 arrest in Daudi cells which is another cell line of Burkitt's lymphoma (Liu et al., 2005). Deguelin also induces apoptosis by increasing Bax protein expression and down-regulating Bcl-2 protein expression (Bai et al., 2013) and also by suppressing PI3K/Akt signaling (Baba et al., 2015). In this issue of *EBioMedicine*, Yu et al. investigated deguelin's novel anti-tumor targets (Yu et al., 2017-this issue). Deguelin inhibited Aurora B serine/threonine kinase activity by directory docking into the ATP-binding pocket, reducing proliferation, anchorage-independent growth, and tumor development in a xenograft mouse model using esophageal squamous cell carcinoma (SCC) cell lines. Importantly, they also found that high levels of Aurora B expression in tumors were correlated with poor overall survival rate in patients with esophageal SCC. Despite the development of conventional therapies like surgery, radiation and chemotherapy, 5-year relative survival rates of esophageal SCC remain poor and esophageal SCC is associated with a high mortality rate. Therefore, Aurora B kinase is a suitable therapeutic target for esophageal SCC and deguelin is a good candidate to treat these cancer patients.

Aurora B Kinase is known to be associated with 14-3-3 proteins, for example targeting Raf-1, Bcr, and Cdc25 phosphatase. Deguelin has the potential to impair 14-3-3 protein function through inhibition of Aurora B function. Deguelin can induce partial synchronization of cancer cells in the most radio-or DNA damaging agents-sensitive to G_2-M phase, although it needs further work whether deguelin induced G_2-M phase cell cycle arrest in various esophageal SCC cell lines, because deguelin-induced cell cycle arrest seems to vary in various cancer cell lines, as mentioned above. Hoellein et al. (2011) showed that combining the epidermal growth factor (EGFR)-targeted agent cetuximab with a pan-Aurora kinase inhibitor, overcomes cetuximab resistance. In addition, inhibition of Aurora B kinase increases radiosensitivity (Clémenson et al., 2017). Taken together, deguelin may be a double sensitizer for cetuximab and conventional chemotherapy/radiotherapy, respectively. Thus, this study provides the basis for novel combination therapy such as deguelin plus cetuximab plus conventional chemotherapy/radiotherapy in esophageal SCC.

Conflict of Interest

All the authors have no conflict of interest to declare.

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DOI of original article: https://doi.org/10.1016/j.ebiom.2017.10.030.
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https://doi.org/10.1016/j.ebiom.2017.11.010
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