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Interactions between Thyroid and Growth Factors during Development

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COMMENTARY

Thyroid hormones (THs) show acrucialactions during the normal development (El-bakry et al., 2010; Ahmed, 2011, 2012a,b, 2013, 2014, 2015a-c, 2016a-d, 2017a-u, 2018; Ahmed et al., 2008, 2010, 2012, 2013a,b, 2014, 2015a,b, 2018; Ahmed and Ahmed, 2012; Ahmed and Incerpi, 2013;Van Hercket al., 2013; Ahmed and El-Gareib, 2014,Incerpi et al., 2014; Candelotti et al., 2015; De Vito et al., 2015; El-Ghareeb et al., 2016; Ahmed and El-Gareib, 2017), particularly growth factors such as insulin-growth factor (IGF-1), fibroblast-growth factor (FGF), transforming growth factor-α (TGF-α), and epidermal-growth factor (EGF) (Candelotti et al., 2015). Indeed, integrin αvβ3 is a co-receptor for these growth factors (Saegusa et al., 2009; Ieguchi et al., 2010). Otherwise, these growth factors may stimulate the release of THs, and generally the development (Ahmed et al., 2015a; Candelotti et al., 2015; Ahmed, 2016d). In addition, vascular endothelial growth factor (VEGF), FGF, and basic fibroblast growth factor (bFGF) might prompt THs-induced angiogenesis in the cardiac tissue (Wang et al., 2004; Zheng et al., 2004). Also, angiogenesis depends on integrin αvβ3 of both endothelial and vascular smooth muscle cells (Bergh et al., 2005; Candelotti et al., 2015). Thus, angiogenesis seems to be a good example of the complex interactions between THs and growth factors.

On the other hand, it has been confirmed by the group of Takada and Takada that an integrin-binding defective-FGF1 mutant (R50E) profoundly decreased the ability of the growth factor to induce cell proliferation and migration, even though R50E did provide increase to FGFR1 phosphorylation and downstream protein kinase B (AKT) and activated protein kinase (ERK1/2) (Ieguchi et al., 2010). In addition, Mori et al. (2008) suggested that there is a direct crosstalk between the integrin αvβ3 and FGF. Also, Saegusa et al. (2009) and Ieguchi et al. (2010) concluded that the binding of integrin αvβ3 plays an important role in the signaling of growth factors, particularly EGF and IGF-1. Other members of the EGF family are neuregulins (NRGs) that are binding to integrins. This binding is vital for the effective growth factor signaling (Ieguchi et al., 2010). In addition, Ieguchi and co-researchers in a great experiment found that the direct associations between NRG1 and integrin αvβ3 were significant for the activation of the ErbB receptor-tyrosine kinases resulting in downstream signaling activation of Akt and ERK1/2 (Ieguchi et al., 2010). Thus, different growth factors may compete for interaction with the same integrin (Candelotti et al., 2015). Additionally, Shih et al. (2004) reported that thyroid (T4) has the ability to increase EGF and TGF-α-induced MAPK activation in HeLa cells that lacked thyroid receptors (TRs). However, NRGs are implicated in several diseases such as schizophrenia, cancer and cardiovascular disorders (Candelotti et al., 2015). Collectively, my group (Candelotti et al., 2015) reported that understanding the role of THs in this crosstalk may facilitate the development of new tools for therapeutic intervention, and in this context the nanotetrac formulation appears to be very promising. Additional studies are wanted to identify the crosstalk between THs and growth factors to prove the efficacy of new pharmacological drugs.

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