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## Comparison of the Dietary Supplement Protandim and 4-Hydroxytamoxifen on Pre-malignant Human Breast Cancer Cells in 3D Culture

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Protandim is a dietary supplement with potent antioxidant properties. We hypothesized that Protandim would inhibit malignant progression of ductal carcinoma in situ (DCIS). A pre-malignant human breast cancer cell line (MCF10DCIS.com) was grown in collagen type I for 1 week and then cultured for 2 more weeks in the presence or absence of a growth factor (GF) combination of TGF-beta and CXCL12, 20ng/mL each. In the presence of GF, most cells exhibited long processes and formed interlacing networks and stellate aggregates. Numerous genes and cytokines involved in cancer progression, inflammation, and differentiation were up-regulated. Bipotency was verified by IHC for pancytokeratin and alpha smooth muscle actin. Additional groups were dosed with 4-hydroxytamoxifen (2.5 micromolar), Protandim (8 micrograms/mL), or vehicle (0.1% DMSO). In the Protandim and 4-hydroxytamoxifen groups, more cells displayed a rounded shape with fewer processes. In the cytokine array, the following decreases by Protandim and 4-hydroxytamoxifen (respectively) were observed: platelet-derived growth factor (PDGF): 55% & 27%; interleukin 5 (IL-5): 81% & 76%; monocyte chemotactic protein1 (MCP-1): 84% & 76%; angiogenin: 68% & 77%; granulocyte-macrophage colony-stimulating factor (GM-CSF): 63% & 44%; interleukin 6 (IL-6): 77% & 79%. These results suggest Protandim may suppress DCIS progression. (NIH/NCRR)