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Suppression of Wnt1-induced mammary tumor growth and lower serum insulin in offspring exposed to maternal blueberry diet suggest early dietary influence on

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Abstract: Abstract Despite the well-accepted notion that early maternal influences persist beyond fetal life and may underlie many adult diseases, the risks imposed by the maternal environment on breast cancer development and underlying biological mechanisms remain poorly understood. In this study, we investigated whether early exposure to blueberry (BB) via maternal diet alters oncogene Wnt1-induced mammary tumorigenesis in offspring. Wnt1-transgenic female mice were exposed to maternal Casein (CAS, control) or blueberry-supplemented (CAS + 3%BB) diets throughout pregnancy and lactation. Offspring were weaned to CAS and mammary tumor development was followed until age 8 months. Tumor incidence and latency were similar for both groups; however, tumor weight at killing and tumor volume within 2 weeks of initial detection were lower (by 50 and 60%, respectively) in offspring of BB- versus control-fed dams. Dietary BB exposure beginning at weaning did not alter mammary tumor parameters. Tumors from maternal BB-exposed offspring showed higher tumor suppressor (Pten and Cdh1) and lower proproliferative (Ccnd1), anti-apoptotic (Bcl2) and proangiogenic (Figf, Flt1 and Ephb4) transcript levels, and displayed attenuated microvessel density. Expression of Pten and Cdh1 genes was also higher in mammary tissues of maternal BB-exposed offspring. Mammary tissues and tumors of maternal BB-exposed offspring showed increased chromatin-modifying enzyme Dnmt1 and Ezh2 transcript levels. Body weight, serum insulin and serum leptin/adiponectin ratio were lower for maternal BB-exposed than control tumor-bearing offspring. Tumor weights and serum insulin were positively correlated. Results suggest that dietary influences on the maternal environment contribute to key developmental programs in the mammary gland to modify breast cancer outcome in adult progeny.