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**Metformin for the Treatment of Breast Ductal Carcinoma In Situ (DCIS)**

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**Lead Organization:** Baylor College of Medicine

**Awarded:** $450,000.00

**Grant Mechanism:** Career Catalyst Research Grant

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**Public Abstract:**

OVERVIEW. It has become clear that altered cell metabolism is a fundamental difference between normal and cancer cells (including DCIS and breast cancer). Metformin is the most widely used oral diabetes drug in the world, and has an established safety profile. Evidence from us and others strongly suggests metformin has anti-tumor activity in breast cancer, but whether this is also true for DCIS is unknown. Metformin is believed to act by altering cell metabolism, but how it does so is poorly understood. In this proposal, we will evaluate whether metformin has anti-tumor activity in DCIS. We will also determine the key metabolic changes underlying metformin’s anti-tumor activity. By understanding metformin’s metabolic mechanism of action, we will be able to use metformin and related metabolic drugs for treatment of DCIS and chemoprevention of DCIS/breast cancer. As metformin is an approved drug with a proven safety record, it should be feasible to move these studies from the lab to the clinic within the next 10 years. Indeed, the results of this study will be immediately applicable to the design an adjuvant therapy trial for patients with DCIS. In addition, this study will help establish the framework needed to develop future novel metabolism-based DCIS and breast cancer therapies.

IMPORTANCE TO PATIENTS AND SURVIVORS. This research is of fundamental importance to the breast cancer patient and survivor community, for the following reasons. (1) It will develop metformin as a therapeutic option for ER-negative DCIS, for which there is currently no adjuvant drug therapy offered. This is especially important, as ER-negative DCIS is the likely precursor to ER-negative and triple negative breast cancers (TNBC), which are among the poorest prognosis groups. In addition, metformin causes relatively few side effects, so it is likely to offer high benefit with low toxicity. (2) With regard to point (1), it is expected that Komen CCR Grant study will lead directly to the design of a chemoprevention trial in DCIS patients. (3) It will lead to an understanding of metformin’s metabolic mechanism of action in DCIS and breast cancer. This is important, as it will allow us to understand the best way to use metformin, both alone and in combination, for the treatment of DCIS and chemoprevention of DCIS/breast cancer. (4) Understanding the mechanism of action may identify new metabolic targets that can be exploited for novel drug development, or for repurposing already known drugs that hit these metabolic targets.