**Institute for Diabetes and Cancer IDC**

**Highlight / Publication:**
Rios Garcia, M., Steinbauer, B., Srivastava, K., Singhal, M., Mattijssen, F., Maida, A., Christian, S., Hess-Stumpp, H., Augustin, H.G., Müller-Decker, K., Nawroth, P.P., **Herzig, S.***, and Berriel Diaz, M. *. 2017. Acetyl-CoA Carboxylase 1-dependent protein acetylation controls breast cancer metastasis and recurrence. Cell Metab. 26: 842-855; * joint authorship IF 18

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**Keywords:**
Breast cancer, metastasis, lipid metabolism, leptin

**Central statement of the highlight in one sentence:**
Our work identified a previously unknown connection between leptin signaling and breast cancer metastasis formation via the regulation of tumor cell lipid metabolism and transcription factor post-translational modification.

**Text of the highlight:**
Breast tumor recurrence and metastasis represent main causes of cancer-related death in women, and effective treatment options are still lacking to date. Here, we define the lipogenic enzyme Acetyl-CoA Carboxylase (ACC) 1 as a key player in breast cancer metastasis. In particular, ACC1 phosphorylation was found to be increased in invading cells both in murine and human breast cancer models, serving as a joint point-of-convergence for leptin and transforming growth factor (TGF) beta systemic cues. ACC1 phosphorylation under these conditions was mediated by TGFbeta-activated kinase (TAK) 1, and ACC1 inhibition was indispensable for the elevation of cellular acetyl-CoA, the subsequent increase in total protein and Smad2 transcription factor acetylation and activation, and ultimately epithelial-mesenchymal transition and metastasis induction. Indeed, both pharmacological and genetic ACC1 deficiency worsened tumor recurrence rates upon primary tumor resection in mice, and ACC1 phosphorylation levels correlated with metastatic potential in human breast and lung cancer patients. Given the also demonstrated principal effectiveness of anti-leptin receptor antibody treatment in halting ACC1-dependent tumor invasiveness, our work proposes a novel “metabolocentric” approach towards metastatic breast cancer therapy.

**Taking account of the HMGU mission:**
The identification of molecular mechanisms in the control of diabetic long-term complications including cancer risk and aggressiveness is at the center of diabetes research and a key target in new therapeutic options.

**The internal HMGU co-operation partners with whom the highlight was compiled, if appropriate:**
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