## Illuminate PROC

### Glucocorticoid receptor activation and chemotherapy resistance

By activating the glucocorticoid receptor, cortisol can promote tumor progression by suppressing pro-apoptotic pathways used by cytotoxic agents.<sup>1</sup>







# GR activation by cortisol<sup>2</sup>

When activated by cortisol, the glucocorticoid receptor translocates to the nucleus.<sup>1</sup>

## Anti-apoptotic gene expression<sup>2</sup>

In the nucleus, activated glucocorticoid receptor promotes expression of anti-apoptotic genes, including *SGK1* and *DUSP1*.<sup>1</sup>

#### Apoptotic suppression<sup>1</sup>

*SGK1* and *DUSP1* suppress apoptotic pathways and can reduce chemotherapy efficacy.<sup>1</sup>

# Illuminate PROC

### Glucocorticoid receptor activation starts with cortisol

#### The stress hormone

Cortisol, commonly known as the stress hormone, is an endogenous glucocorticoid that plays an important role in a range of cellular and physiological functions.<sup>3</sup>

#### GR activation in cancer

By activating the glucocorticoid receptor (GR), cortisol can promote tumor progression by suppressing pro-apoptotic pathways used by cytotoxic agents.<sup>1</sup>

High glucocorticoid receptor expression in ovarian cancer correlates with shorter progression-free survival, and it has been shown in preclinical studies that physiological cortisol levels suppress chemotherapy-mediated cell death.<sup>1,4-6</sup>

Evidence suggests GR

activation has a key role

in treatment resistance<sup>1</sup>

Emerging research brings hope for clearer understanding. New science is shedding light on mechanisms of resistance. Studies have shown that chemotherapy activity can be limited by cortisol-driven activation of the glucocorticoid receptor, even at physiological levels of cortisol.<sup>1</sup>

Cortisol

#### Scan to illuminate more





References: 1. Colombo N, Van Gorp T, Matulonis UA, et al. *J Clin Oncol.* 2023;41(30):4779-4789. 2. Buonaiuto R, Neola G, Cecere SC, et al. *Biomolecules.* 2023;13(4):653. 3. Thau L, Gandhi J, Sharma S. Physiology, Cortisol. In: *StatPearls.* Treasure Island, FL (per AMA) : StatPearls Publishing; August 28, 2023. 4. Veneris JT, Darcy KM, Mhawech-Fauceglia P, et al. *Gynecol Oncol.* 2017;146(1):153-160. 5. Greenstein AE, Hunt HJ. *Oncotarget.* 2021;12:1243-1255. 6. Greenstein AE, Hunt HJ. *Int Immunopharmacol.* 2023;120:110312.

Copyright @ 2025 Corcept Therapeutics Incorporated. All rights reserved. DSE-01247  $\,$  FEB 2025 ONC  $\,$