

## SPEAKER Q&A

# Pearlie Epling-Burnette

In anticipation of the upcoming European Protein Degradation Congress, we caught up with Pearlie Epling-Burnette from the Department of Immunology at the Moffitt Cancer Center. She gave us a glimpse into the application of PROTACs to target immune regulation before she takes to the stage in Basel this May.



Pearlie Epling-Burnette  
Professor, Department  
of Immunology  
Moffitt Cancer Center



### Please can you kindly introduce yourself

I am a Senior Member and Professor at the Moffitt Cancer Center & Research Institute, Tampa, FL. Moffitt Cancer Center & Research Institute is a National Cancer Institute (NCI)-designated Comprehensive Cancer Center recognized for its scientific excellence in the state of Florida, USA. It is a freestanding organization supporting both research and clinical activities. As a member of the Immunology Program, I have made several leading observations on immune deregulations in the setting of bone marrow failure and hematological malignancies, and solid tumors.

### What will you be talking about at the European Protein Degradation Congress?

Cereblon (CRBN) has been almost exclusively studied as the molecular target of immunomodulatory drugs (IMiDs), including thalidomide and its immunomodulatory derivatives, and as such the physiological roles of CRBN are poorly characterized. Using *Crbn*<sup>-/-</sup> mice, we show that CRBN controls the metabolic phenotype of CD8<sup>+</sup> T cells through a previously unappreciated mechanism.

While mouse CRBN has a single amino acid substitution that quenches IMiD compound activity, we find that its E3 ubiquitin conjugating function is conserved when engaged by other classes of protein degraders.

### Why is targeted protein degradation exciting the field?

Targeted protein degradation offers a unique opportunity to modify the human proteome for both research and therapeutic purposes.

### Apart from oncology, which other therapeutic areas are of interest for adopting PROTACs?

We are interested in the application of PROTACs for immune regulation.

### What's your (team's) main area of focus relating to PROTACs/ Molecular glues?

We are evaluating basic mechanisms associated with proteins that are exploited for PROTAC therapeutic development. This may provide an avenue to improve PROTAC small molecules and understand adverse events once the products are developed clinically.

### What key technologies are required to identify proteins for degradation?

Chemistry, screening technologies, ubiquitin assays, biology relevant to the degraders.

### If as the industry hopes, the Arvinas trial is a huge success, what does this mean for the industry?

#### What next?

There will be a huge commercial interest in developing novel therapies based on the PROTAC concept.

### What are your thoughts on how to retain PROTAC potency along with selectivity over other targets?

This is an emerging field with a lot to be learned.

### Are there any other research areas within pharma that you find as exciting as targeted protein degradation?

No, protein degraders are a fascinating new research arena with a lot to be learned.

Connect with Pearlie at the European Protein Degradation Congress this May 22-23rd 2019 in Basel, Switzerland.

VIEW  
AGENDA

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