Department of Biological Sciences Seminar Blog

Seminar Date: 1/20/17
Speaker: Dr. Chris Burd, Yale University
Title: *"Arrestin(g) insights into regulation of protein sorting in the endosomal system"*

Membranes: They're a lot more complicated than you think.

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Background info

This January 20, 2017 Department of Biological Sciences seminar featured Dr. Chris Burd (http://medicine.yale.edu/lab/burd/) from Yale School of Medicine. His lab focuses on understanding the assembly and maintenance of organelles in the endomembrane system. His seminar was titled *"Arrestin(g) insights into regulation of protein sorting in the endosomal system".*

***What** does this mean?*

Most people know what the cell membrane is; it's what separates the inside of the cell from the rest of the environment. Well, the endomembrane system, specifically the secretory pathway, (http://www.cureffi.org/2013/02/24/cell-biology-04-the-secretory-pathway/)
acts as a cell membrane but for organelles i.e. the endoplasmic reticulum, the Golgi apparatus, lysosomes, and the vesicles.
The endomembrane system is responsible for synthesizing and arranging these organelles in the cell.
It is constantly reacting to the environment and is continually being remodeled. So, it must be tightly regulated through various cellular mechanisms.

***What** do they want to know?*

Scientists know the secretory pathway's general purpose, but the question of *how* the system works is still unanswered.
What machinery is needed? I.e. what proteins & what is it that regulates them?

***Why** do they want to know it?*
When this pathway doesn't function properly it can lead to several major diseases... Think: cancer, neurodegenerative disease (e.g. Alzheimer's and Parkinson's disease), & some infectious diseases.

***How** do they accomplish this?*
They use *Saccharomyces cerevisiae,* commonly known as the baker's yeast, as a model organism in order to probe the endosomal system through molecular techniques. These techniques give insights to the mechanisms behind the sorting & trafficking pathways.
Think: genetics (https://en.wikipedia.org/wiki/Genetics)/genomics (https://en.wikipedia.org/wiki/Genomics) proteomics (https://en.wikipedia.org/wiki/Proteomics)
biochemistry, and live fluorescence microscopy (https://en.wikipedia.org/wiki/Fluorescence_microscope).

Initial THOUGHTS
When I first read the title for Dr. Burd's presentation, I was pleased to see he would be presenting on Arrestins, (https://en.wikipedia.org/wiki/Arrestin)
also known as trafficking adaptors.

"Arrestin(g) insights into regulation of protein sorting in the endosomal system"

WHY?
Because I just spent the last 10+ weeks working on a project that was centered on understanding how alpha-arrestins function as trafficking

adaptors. Needless to say I was excited to learn more & pretty happy I was well versed in the conversation.

JUST KIDDING!
As I started to dig into Dr. Burd's previous research & publications (http://medicine.yale.edu/lab/burd/publications/),
I realized there was very little talk of arrestins & a quick *cntl + f* in his recent papers confirmed that arrestins were a new topic in his lab.

YUP
That is precisely what happened.
Luckily, I was fortunate enough to have lunch with Dr. Burd before his presentation. As the conversation flowed it was stimulating to hear how his research was shifting from lipid trafficking of the endomembrane to discovering more about an arrestin-like protein that promotes trafficking within the endosome membrane.
Knowing that it's OK & possible to branch out within your field of study was refreshing to hear. It's encouraging as a young scientist to know that you can spend 10+ years focused in one area, but then all of a sudden branch out & discover something new.
PLUS as a fellow lover of baker's yeast, it's great to hear of all the opportunities & possibilities these little guys have to offer.

The talk
Arrestin(g) insights into regulation of protein sorting in the endosomal system

Membranes are tightly controlled & always changing. Meaning, they have the ability to sort and direct molecules 24/7. Recycling pathways, retrograde pathways,
(https://en.wikipedia.org/wiki/Retrograde_signaling)
& degradation pathways are constantly being used to keep up with its environment.

EXPERIMENT

They focused on an iron channel in the membrane (Frts1/Fet3: allows for iron to come in & out of the cell). When concentration of iron was low – there were many channels present. However, when concentrations of iron were high – the number of channels greatly decreased.

How did the cell respond to its environment? To answer this, they screened different mutations that counteracted the effect of iron on channel expression.

All gene screens led to a retromer-sorting complex, which is a protein complex that functions to export cargo from the endosome. It is made up of three proteins & is allegedly responsible for packaging cargo into vehicles.

REMEMBER – we care because if this doesn't function properly is could lead to late onset Alzheimer & Parkinson's disease.

Results

How does this retromer get to the endosome? Turns out the proteins that make it up all have a similar domain, which allows for it to directly bind. One protein they looked at specifically within the retromer-sorting complex was the Vps26.

Through various tests they discovered that this protein functions much like an arrestin would. An arrestin is a trafficking adaptor so it can be thought of as the switch that controls whether the iron channels are present in low or high concentrations. The arrestin does this by responding to the environment. For example, when the iron concentrations are high it will ubiquitinate, or mark the iron channel for endocytosis and thus there will be fewer iron channels in the membrane.

This work has allowed Dr. Burd and his team to gain more insight into the mechanisms that control the membrane.

TAKE AWAY

My initial thoughts were something like "*wow I have so much more to learn,"* but there were several times when I knew exactly what Dr. Burd was referring to, especially during lunch, which was pretty exciting. I have recently found that one of the most exciting things about science is that revelation when you start to make connections & truly understand what you're talking about.
Overall, his talk was thought-provoking and I left with a feeling of awe and excitement to see what more I can learn in the molecular biology field.