

A Workflow for Academic Drug Discovery

Baylor College of Medicine Customer Case



On one of the top floors in the Baylor College of Medicine Neurological Research Institute, I visited the Center for Drug Discovery to learn from the Director and Medicinal Chemistry Leader, Dr. Justin Anglin, about muscle cachexia as well as their innovative projects focused on male contraceptives. We were able to take a tour of their state-of-the-art lab after which includes a full suite of Biotage products, something Dr. Anglin uses every day.

Dr. Justin Anglin is Director and Medicinal Chemistry Leader at the Center for Drug Discovery, Baylor College of Medicine Neurological Research Institute.

By Sarah Moran

Can you describe your current projects?

We're working on inhibition of kinase targets for various muscle cachexia, or muscle-wasting. There is a big push for muscle cachexia, for example people who sit in a hospital bed all day and begin to lose their muscle. These tests will hopefully identify a drug that will induce muscle growth and reverse atrophy. We think that inhibiting these kinases will help reverse the disease stage because they're the primary signaling mechanism for myostatin, which inhibits muscle growth. Our entire suite of Biotage products are used on this specific project.

We're also working on a project focused on male contraceptives. Marty Matzuk is the director of the center and it's one of his biggest projects. He's identified dozens of potential drug targets by doing gene knock-out across the whole genome. He knows which genes are spermatogenesis-specific and we're

methodically screening these for small-molecule ligands using our DNA-encoded chemical library collection, now past three billion in total number of unique molecules. The idea is to find a safe, orally available drug for male contraception that can be used in conjunction with female contraception. People are reacting positively to it because it encourages trust between the two partners and adds another layer of protection to their lives.

As a director, how much are you in the lab these days?

Constantly, we're currently working through projects and for everyone in the lab is all hands on deck. I'm the one that assigns the projects, but I'm still an active part of the work inside the lab. We have five chemists in-house in addition to me, so some of the projects include all of us, but the majority of them are on a more individual basis. We even do some partnerships with other labs around the state of Texas.

How many of your projects require flash chromatography?

100% of them. In addition to the medchem projects, I have all externally-sourced probes, inhibitors, etcetera go through my group so that QC work is done and purification through Biotage instruments to ensure purity.

Since you are a practicing medicinal chemist, I would imagine flash chromatography is important in your research?

It is extremely important, you can't do any medchem projects without strict-quality control. The risk of being misled is just too high. Using the Isolera plus the columns allows us to have super clean results on our high-resolution mass-spec and NMR spectra and, ultimately, confidence in our assay results.

What factors do you consider when choosing tools to use in your lab?

For me it's always the Isolera. I might use something else if I dry-load but liquid loading is generally sufficient and expedient, and that means the Isolera. I'll use it in combo with the V-10 Touch because it's efficient and fast to use them together.

How has your workflow been impacted by these tools?

The technology we have at Baylor is a great blend of chemistry and biology. Our DNA-encoded library screening is great, but there's always a ton of compounds that need to be confirmed from this process. Biotage instruments are indispensable in the lab towards this end. Using the entire workflow, we're able to do things more efficiently. I can run eight samples in the microwave at one an hour, whereas before, it would take me over twelve hours to run eight samples. I can knock out 16 purifications with the Isolera and then dry them on the V-10 quicker than using a rotavap and round-bottom flasks without risk of solvent bumping. I use the entire Biotage suite when working in the lab. With the Isoleras we setup for reverse-phase, I tend to use the 13 x 100 racks such that fractions are eight milliliters. The V-10 Touch dries these in a 20 mL bottle under 10 minutes with minimal heating; it's a great setup.

“With using the entire workflow, we're able to do things more efficiently



"For me it's always the Isolera." All of Dr. Anglin's projects involve flash chromatography at some point.



The quickest route to dry product. "I can knock out 16 purifications with the Isolera and then dry them on the V-10 quicker than using a rotavap and round-bottom flasks without risk of solvent bumping."

How often are you using Biotage products/ equipment in your day-to-day activities?

Constantly, I'd take the Isolera home with me if I could. It's hard not to use it!

In this university setting, how do you work with students in your research?

I have one undergraduate student from Rice University who is very bright and she uses the Biotage instruments, they're super easy to use and now she's in love with them too. I have another student who is on a rotation from the Biology department and he's learning the medchem process. We also have summer students from various schools around the country as part of a SMARTS program at BCM. We're largely research oriented when it comes to the medical school, so we don't always have full-on

chemistry students coming through. I think it's somewhat of a shock for students not acquainted with a medchem to see such a setup, especially coming from teaching labs. They quickly catch on to use of the Biotage instruments, it's quite simple for them to understand as a complement to their understanding of chromatography from classes.

What is next on your wish list for increased success with your research projects?

I absolutely want the carousel for the V-10 Touch, I won't get tennis elbow with it! I'd love to get another V-10 Touch just to add to our suite. I saw a demo of the new Biotage Selekt with Brian Mercer last week and it's on the list, but with all of our Isoleras, that might be a while for us! I really like the barcode scanner as well for the new columns, the entire machine is snazzier. We're also looking at the Alstra peptide synthesizer such that we don't have to merge two pipelines onto our existing Initiator+.

Dr. Justin Anglin's Favourite Features on Biotage Systems

Biotage® Initiator+

- » Queue up runs (sets of 8)
- » Reactions are fast

Isolera™

- » Lots of options with control
 - » Fraction size
 - » Wavelengths
 - » Number of racks
 - » Use of 3+ solvents in same run
- » Ease of use
- » Can save methods

Biotage® V-10 Touch

- » Quick dry times
- » Does reverse-phase super well

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