

## Headline Patrol Companion Guide

Here's a short companion guide to the March 30th episode of U2FP CureCast, a conversation that included Matthew Rodreick, Jason Stoffer and me about ways to hype-check spinal cord injury research news seen in the press or online. We offer a few basic filters to sort out discoveries or clinical reports that have scientific validity and real human promise from overheated public relations releases or click bait.

First off, don't swoon for headlines that contain words such as "breakthrough," or "miracle," or even "cure." Such editorial enthusiasm can distort your expectations. Be a savvy information seeker, try to sort the gold from the glitter, keep your mind open, expect progress and hope for the best, but remain healthily skeptical.

The story should tell you straight away if it's a preclinical study – which means it treated animals -- or if it's a clinical stage study – using humans.

If the news report concerns animals, which animal? Mice and rats are quite commonly used to test drugs or cells, but these little guys very often show measurable recovery that later does not translate to larger species, e.g., humans. So always read a rodent study with a healthy dose of skepticism.

Also, regarding animals, how is the injury modeled? Human SCI is almost always due to a contusion, or bruise, on the spinal cord. Animal experiments often try to simulate the human spinal cord crush, but sometimes use compression or a full-on slice or partial slice. Just keep in mind that animals with spinal cord injury don't really correlate with people.

### Human studies

Now if the study enrolls humans, the most critical question is what is the treatment timeline? Is the story talking about an acute therapy, administered in the hours or days after injury, or does it apply to people living with SCI?

(Here at U2FP the emphasis is on the chronic injury. That's not to say acute studies are not essential but they are obviously of little consequence to the SCI community.)

Now, which people are being treated? What level of injury? Many studies avoid treating cervical injuries for fear that a negative effect could cause a person to lose already limited function. Other studies only want to treat cervical injuries – there are better ways to measure a treatment effect in hand or finger function than a mid-body improvement.

Complete or incomplete? You always have to ask, and it's a fair question, would the person have gotten better without treatment. We all know this happens. But it is much more likely to happen in those considered incomplete.

Jargon alert: Scientists who work with human SCI often refer to the AIS scale to gauge the level of a person's impairment. AIS A means no motor function, no sensory below the injury lesion area. AIS B adds sensory, C adds some motor and D means the person can move the legs and perhaps walk. News reporters sometimes don't look at these scores and therefore "paralyzed man walks" headlines are distorted from the get-go.

If the therapy being studied uses cells, what is the source? Maybe the cells are from the patients' own bodies; maybe they were processed from an embryo, or fetus, or engineered using genetic coding. This could make a difference in whether a patient has to take immunosuppressive drugs, and there could be ethical issues for some people regarding cell source.

Another important question regards the role of rehabilitation or training in the study. If there was an aggressive rehab piece, was it the reason there was an effect and not because of the drug or device?

It's important to understand the source of the news you're reading. Is there a byline and a news affiliation noted? Quite often no author credit is given because the news originated in the public relations office of a university. A real reporter will ask people outside the academic silo to comment on the study or offer broader context.

The news story or release probably won't get into the study design too much, so I always get hold of the research study that the news article is based on. These are not always available without a paywall, alas. See <https://pubmed.ncbi.nlm.nih.gov/> to look up studies by author or subject.

You may come across a study that involves a single patient, a so-called "N of 1." Don't let a reporter let the researchers sell you too hard – these types of studies may help establish a concept but are far from the level of proof needed in medicine.

Other considerations: was the study executed with rigorous scientific standards, e.g., was it controlled (with a group that got the treatment compared to one that got placebo), was it blinded so neither patient nor researcher knows who got what?

Another important question in all research: what is the mechanism of action for the drug, cell transplant or device? Maybe the investigators don't know, but it's important for reporters to ask scientists to explain or at least speculate.

### **What does the research team mean by significant?**

Scientists may say a treatment effect was significant – but what do they mean, statistical significance or real, meaningful effect on function.

For example, a study may say a group of animals improve on a 21-point functional measure called the BBB from 6 to 12. Wow, a 100 percent increase in function! There was an effect, yes,

but that doesn't mean there was meaningful recovery. The BBB 12 animals still have paralyzed hindlimbs.

I spoke with Marquette University SCI scientist Murray Blackmore about this, and he hammers the point:

The difference between “statistically significant,” and “significant” trips up communication between scientists and the press, and in turn with the public. Findings get reported as statistically significant and people can misunderstand what that means – readers need to be reminded that effects can be very small but still described correctly as “significant”

I also asked John Houle about claims of significance. He's a senior SCI scientist at Drexel, and a member of the U2FP Scientific Advisory Board. He agrees it is important for a news story to tell you how recovery of function was defined.

Are there several tests performed and do they examine general and specific tasks? Is there a direct demonstration that the therapeutic approach is responsible for the recovery? Has it been replicated by the authors in a sufficient number of animals?

Replication is indeed an essential part of scientific inquiry – a treatment or therapy has to work in the hands of others. But replication seldom happens in SCI research and when it does, the second lab, following as explicit a recipe for the experiment as possible, almost never gets a therapy to work the way the first lab did.

Blackmore further comments about the process of discovery that we don't hear about:

Scientists are obligated to tell the truth and almost always do – but they are under no obligation to tell the whole truth. This seems bizarre but it's how the system works. What makes it into academic journals and into the press are the cherry-picked successes, not the experiments that yielded negative results. If you try a treatment in three different kinds of injuries, and you only see a positive result in one, it doesn't break any rules to report only the positive and never mention the negatives.

“Readers need to realize,” says Blackmore, “that the media may report what a treatment CAN do, but what it CAN'T do is often buried in a lab drawer somewhere. So, people should be asking about the limits of efficacy.”

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