Marie: Hello and welcome to *The Parkinson’s Research Podcast: New Discoveries in Neuroscience*. I'm your host, Dr. Marie McNeely, and I've partnered with The Michael J. Fox Foundation for Parkinson's Research to bring you to the forefront of the field of neuroscience to discuss the latest advances and discoveries with leading experts.

The Michael J. Fox Foundation created this podcast for researchers, clinicians, and industry professionals with the hope that these conversations and the resources that we share will advance your efforts and partnerships to improve brain health. We are welcoming guests with a range of experiences and viewpoints. The views expressed belong to the guests themselves.

And today we are thrilled to be welcoming our guest, Dr. Nicole Polinski. Listeners, Nicole is Director of Research Resources at The Michael J. Fox Foundation for Parkinson's Research. And today we are excited to talk more about Nicole's role at MJFF and the wide variety of tools that MJFF can provide for researchers. So, Nicole, welcome to our show today. How are you?

Nicole: I'm doing very well. Thank you.

Marie: Well, we are excited to have you here with us. And I'd love to start by talking about your background. So, can you tell us more about what you do there in your current role at MJFF and how you found your way to this position?

Nicole: Sure. So, I have a PhD in neuroscience. I finished my PhD in 2016 and came straight to The Fox Foundation. So, in my PhD research, I was really focusing on biomedical research, specifically preclinical models of Parkinson's disease and age. So, I was already familiar with The Fox Foundation, and it was a natural transition then into the work in Parkinson's disease at the Foundation. Since joining, I worked on our Preclinical Tools and Models Program, and I still am Director of that program today. So, I oversee the strategy, investments in our preclinical tools and models program. I also advise on our Access, Data, and Biospecimens Program, specifically around biospecimen distributions.

Marie: Excellent. And perhaps next we can dive into the details of some of the tools. So, Nicole, can you start by giving us a general overview of the MJFF Tools Program and tell us how it all started?

Nicole: The Fox Foundation is traditionally seen as just a grant funding organization. So, you apply with your ideas for research programs, they're reviewed, they get funded, and you get the money from The Fox Foundation to support your research.
However, we're so much more than this. We really work not only to provide researchers with funding to accelerate their research, but also shared reagents and resources that can speed research, help with looking at reproducibility across studies, and really move the needle faster. So, our Preclinical Tools and Models Program really started around 2010, I would say, 10 years into The Fox Foundation. And it started because in some of the early grants that we were funding, we were seeing a common theme where a lot of projects would either be very slow to start or would have a hard time getting off the ground because they didn't have the right tools and models available to them. So, they would either spend a lot of time trying to use suboptimal tools in the project, which would cause delays, or they'd have to start by generating the tools and models themselves.

And really we were spinning our wheels spending a lot of time and money on those initial reagent and resource development programs within each individual project. So, seeing that pattern, we decided to take a step back and focus holistically on addressing this issue. So, we started our Preclinical Tools and Models Program, which really looks at generating high quality, open access research tools and models that researchers in academic and industry groups can access for their research. So, making sure everything is high-quality, validated, easy to access, and available to nonprofit as well as for profit groups.

Just a little more detail. We focus across the board on different tools related to different targets in Parkinson's disease. So, genetic targets like LRRK2 and GBA, pathology targets like synuclein, mitochondrial targets, inflammation, really you name it, we include it.

And the types of tools and models we focus on really span detection reagents such as antibodies to models like IPS cells, immortalized cell lines, rodent lines, to things like compounds, and viral vectors, and proteins. So, we're really focusing on trying to address the field-wide gaps and challenges that the community is facing by developing and distributing these resources.

Marie: Certainly. And Nicole, I think this program really fills an important need in the field. And I'm really glad that The Michael J. Fox Foundation is addressing some of these major gaps in the field that, like you said, can often hinder research projects and make it difficult to get started. So, what are some of the key pillars of this program, and perhaps, how has it evolved over the years since 2010 when it was launched?

Nicole: This program, really our key pillars are providing reagents at an affordable cost to researchers and non-profit and for-profit groups. They need to ideally be available with minimal barriers to access. So, trying to prevent the additional paperwork and licenses one might need in order to access the tools, and making
Nicole: sure the tools are well validated and used in systems that are relevant to Parkinson's disease researchers.

So, you're fully aware when you're looking at the tool on a commercial catalog of how it will perform in your system. And global distribution, I will add. So, those are our key pillars. And really using these pillars, we've had some good success in the program. We have to date over 200 tools available. And since our program really started in 2010, we've distributed over 100,000 units of our tools globally.

Marie: I think that's phenomenal. And then perhaps you can just kind of break down and tell us — this program is comprised of three different focus areas — what are these focus areas, and why was it so important to develop each of these different three areas?

Nicole: So, the three focus areas of this program are our Tool Evaluation Program, our Sponsored Tools Program, and our tool Generation Program. So, starting with the first, our Tool Evaluation Program really seeks to provide better characterization data on tools that are already commercially available. So, folks might be interested in using a reagent, or a tool, or a model, but there's not a lot of data behind it.

They're not really sure if they want to spend all the money to access the tool when it may not work in their hands. So, the program is really focused on providing that additional characterization data that will let the community know, yes, this is a great resource for your research, or we may want to direct future efforts to developing alternatives or better tools for that specific readout or need. So, that's our Tool Evaluation Program.

Our Sponsored Tools Program is then focusing on when reagents and models are developed in academic settings and aren't open access. So, generally, if a tool is developed in an academic institution, it's shared from the PI through MTAs or material transfer agreements. And this paperwork can take a lot of time and energy to process from the PI and the technology transfer office at the university.

The PI has to use their internal resources to keep up stocks to share with other researchers. So, the Sponsored Tools Program really looks to take that burden off of the investigators by moving the tool to a repository that can distribute on their behalf. So, in this case, the institution and the PI still own the tool, but they license the right to distribute it through our Sponsored Tools Program to one of our repositories. And then again, it's made widely available through commercial mechanisms to global research audiences. So, that's our Sponsored Tools Program.
And our last program is our Tool Generation Program. This program really seeks to fill needs where a tool is not available or the commercial tools are lacking and there are no alternatives in academic settings either. So, in this program, we partner with tool manufacturers and academic researchers in Parkinson's disease to develop research tools from scratch to try and stay upstream of intellectual property restrictions and make sure that the tools that we develop are high-quality, made by the best researchers who are poised for success, in a collaborative manner. So, the tool manufacturer is partnering with the Parkinson's disease expert to make sure it's designed well and validated well. And the right characterization data is added to the product page. And then it's, again, made widely available through the commercial distribution mechanisms of the tool generation partner.

Marie: That makes sense. Well, Nicole, that was a fantastic introduction to these three different areas of the program. And I'd love to dig into a little bit of detail about each one if we can. And perhaps we will start with the Tool Generation Program. You gave us an overview of its purpose and why it's so important. But maybe if we could dig into a little bit of the details of how it works and maybe how you select the ideas that go into this Tool Generation Program.

Nicole: So, our Tool Generation Program is really seeking to focus on field-wide needs. So, needs that are shared by research groups in academic and industry labs, and areas that are reagents that would accelerate the research into Parkinson's disease or therapeutic development across numerous hands. So, we're looking at supporting different projects that we hear about and have folks requesting tools, either just through conference attendance and talking to folks and hearing about their research struggles, looking at advancements that are published recently in the literature, and seeing how different reagents and models could take that research advancement to the next stage, or in discussion with folks who are coming to us and saying we've tried X, Y, and Z, and none of it seems to work. And we're really stuck spinning our wheels here.

So, it's a lot of back and forth with the research community, a lot of looking at recent publications, and data sharing. But also folks have the opportunity to email us at tools@michaeljfox.org to suggest tools or just let us know in general what their needs are. So, once we have that initial list of ideas, we really are trying to focus again on the ones that are going to impact a wide variety of labs and fill field-wide gaps.

So, once we've selected those different tools and models that we'd like to pursue, we have to find the right group to make the tool or model. So, we have a network of different companies that we partner with, and we're always open to additional partnerships if different groups have the right technology that would accelerate this project. We find the partner that we want to use to manufacture the tool and
design it, and we couple them with a researcher who has expertise in the target so that they can provide additional reagents and help with validation. They can help design the tool, and they’re really helping us inform our strategy for developing and characterizing the tool. So, it’s a very collaborative process in which we’re working with numerous parties, usually across the for-profit and nonprofit space to really put ourselves in the best position to make a high-quality reagent or model available.

Marie: Very interesting. And perhaps to give us some idea of the scope or the length of time here, what is the timeline? I imagine it varies a little bit from project to project from receiving that suggestion or maybe identifying that global need to when a tool is actually ready to be deployed.

Nicole: That can take a very long time. A lot of times the tools fit into this Tool Generation Program because they’re difficult. There are no commercial alternatives available because groups have tried and failed. So, a lot of times we are pursuing the more challenging, tricky targets and tools of need for the community. And so, it can take quite a bit of time.

We put a lot of effort up front before we even start any research work on the project to make sure that the ownership and intellectual property stream is clear so that when we’re done and we have a tool or model ready, it can be shared widely with minimal barriers to access. So, that can take some time if licenses are needed and The Fox Foundation has to take on that burden. And also we really want to set up the design of the project to increase our chance of success and make sure we’re screening in the right conditions and looking at the right things as we go. So, all in all, it really heavily depends on the target and the tool, but these projects, I would say, generally span a couple of years.

Marie: That makes sense. And thank you for sharing some detail about this Tool Generation Program. Let’s talk next then about the Sponsored Tools Program. So, can you give a little bit more detail on how that program works and perhaps what MJFF is looking for?

Nicole: So, the Sponsored Tools Program usually happens when an academic group has made a research advancement through the generation of a novel model, typically, or another resource and reagent that would be impactful for the community to continue on the efforts of looking at that target or pathway. So, in this program, it’s really identifying tools that are already available in academic settings and then moving that tool to a repository, through negotiations and licensing arrangements, to make sure that folks can access it, and the researcher who generated the tool isn’t burdened with processing requests.
So in that case, we’re looking at, again, tools that would be a field-wide impact. So, reagents that would be used by multiple groups and generally the researcher who owns the tool and model is being burdened by requests that are coming in. So, it’s very similar to our Tool Generation Program. I would say in this case, our Sponsored Tools Program, we’re a little bit more flexible and may pursue here tools that are really suited for academic access because we don’t have as much leeway over the licensing and intellectual property sides. So, there may be additional restrictions for industry access.

Marie: That makes sense. And for listeners out there who might be feeling like they are receiving a burdensome amount of requests, how do people get their tools added to the Sponsored Tools Program?

Nicole: Again, you can feel free to email us at tools@michaeljfox.org. We would love to hear about your reagent and love to help kind of take some of that burden off of you because really we want you focusing on hypothesis-driven research and uncovering new discoveries and potential therapeutic directions for Parkinson’s disease, not acting as a tool or model distributor or manufacturer. So, please feel free to reach out to us and let us know.

Marie: Fantastic. And then the third program that you introduced in the beginning there, the Tool Evaluation Program. Are there additional details about this program that you’d like to share?

Nicole: Yeah. So, I would say this program is a little more flexible. We don’t have as many hard and fast rules around this, but for our Tool Evaluation Program, we have a couple of partnerships that are already underway that are looking at some of the common tool types and providing additional characterization data for the community. So, we have a very interesting partnership with this nonprofit group Icarus, and they’re focusing on providing comprehensive side-by-side characterization of antibodies toward different targets in order to determine which ones may be best-suited for different applications. And so, this takes a lot of the legwork off of the groups who are performing research on those targets by doing a lot of that due diligence and screening ahead of time, so they can point you to the right reagent that’ll get you kick started in your research program.

So, we have an ongoing partnership with them for characterizing antibodies to common Parkinson’s disease-related targets. But in general, if you are interested in suggesting ideas for different tools for us to characterize or you think there’s a gap, but there may or may not be a commercial tool that fills that gap, feel free to always reach out by email at tools@michaeljfox.org, and we’ll help see if there’s room for The Fox Foundation to play in characterizing that different tool.
Marie: Wonderful, and I think this is a theme that has come up in a variety of different conversations with The Michael J. Fox Foundation, just how open the organization is to feedback and having these connections and dialogues with scientists and researchers out there.

Nicole: I agree. I think one of the rate-limiting steps in my position right now is hearing from the community. So, we have the space to continue to generate new tools, make tools more openly available, and characterize tools, but we just need to know which ones you want us to focus on. So, please feel free to reach out.

Marie: Oh, wonderful. And I know the organization has a phenomenal catalog online where researchers can browse the different tools that are available. So, can you talk more, Nicole, about this research tools catalog and why it was created?

Nicole: Sure. So, on our web page under Research Tools, we have a number of different resources that we provide the research community so they can have an idea of some places to start if they're new to Parkinson's disease or interested in focusing on a target they're not so familiar with. So, we have our Research Tools Catalog, and this is a centralized location that lists all the tools that have fallen under our Tool Generation Program or our Sponsored Tools Program. So, you can go in, filter by tool type, filter by target, see what's currently available and what's in development with estimated availability dates for the different tools. So, it's a one-stop shop to kind of understand what our program has done in the past and what we're continuing to do at the present.

We also have other resources available outside of what we do for Tool Generation and Sponsored Tools Programs. So, our Preclinical Tools and Models team has a wealth of knowledge and information on different models for Parkinson's disease. So, we're always open to speaking with folks about the different models, since there are so many, to give folks an idea of a place to start or some different models that may be of interest to them.

We have a Preclinical Models page on our web page for Research Tools, and it gives a sense of the variety of different models out there and some recommendations based on pathway, or symptom you want to model, or target you want to pursue. So, that's another resource out there that is very helpful for the community to really understand kind of the research tool landscape and get a jump start on their research program.

Marie: Definitely, I think that is tremendously valuable because like you said there are over 200 tools, so it can be kind of overwhelming to just sort of scroll through the list and see all these different things. I think that is a wonderful addition, and you mentioned that over 100,000 of these tools have been sent out. Do you have a sense of what some of the most popular or most highly used tools have been?
Nicole: Yeah. So, a couple that come to mind are some of our antibodies that we've generated. So, we have spent a lot of resources and effort in our program to generate high-quality antibodies to different targets for Parkinson's disease.

One example is our phospho Threonine73 Rab 10 antibody. And this antibody is very useful for a number of different applications and looking at this target in a host of different pathways. So, it has been used in, I think last time I checked, around 80 publications since it was made available in the 2017-ish range. So, it's been very popular and very field-enabling for the community and phospho Threonine73 Rab 10 is really now being used as a good readout of LRRK2 kinase activity, both in patients with the LRRK2 mutation and models, but also in the wildtype systems or idiopathic systems where there is no LRRK2 genetic link. So, it's been really useful for the community, and this high quality antibody has really been a very useful tool for investigating that pathway in biology.

Marie: Certainly and I understand that The Michael J. Fox Foundation has some partnerships established for this Research Tools Catalog, particularly for things like antibody validation. So, Nicole, can you tell us more about this?

Nicole: Yeah, our partnerships are really impactful. I think they are what brings the success to the program that we've seen to date. So, we're always very interested in working with the right companies that manufacture and distribute the reagents to make sure that we're poised for success in using the most cutting-edge, best technology for the generation portion of the program but also partnering with groups who have the expertise in the target so that we can really understand the performance of the tool and model, and make sure that we're hitting the field needs that were previously identified.

So, I couldn't even estimate how many partners we've had to date in these different aspects but we're really interested in working with folks who would like to help us characterize the tools that they're nominating and recommending and that have the right systems for validating the tools and models that we make to make sure that they are meeting expectations and are of the highest quality.

Marie: Absolutely. And I know you mentioned the pre-clinical models for PD research previously, and I'd love to talk more about these. I know there are tons of them out there as you mentioned, so what are some of the ones available, and how does an investigator perhaps take the time to choose a model that they're going to use for their research?

Nicole: I think that can sometimes be the hardest step is kind of knowing where to start and what models to look at for folks. And so we, over the years, have generated a lot of internal knowledge on the different types of models out there, the specific
models with their pros and cons, and last year, actually, we embarked on an effort to put all of that on paper so that folks are aware of the different models and can kind of use that to inform their strategy and the design of their study that they want to pursue. So, we have a Pre-clinical Models page on our website that provides the community with an overview of the different types of models out there and then provides recommendations based on the specific target you’re looking at, or the pathway, or the symptom you want to measure that's related to Parkinson's disease.

And this also has links to some of the data sets that we've generated on different models and the partnerships that we have to educate the community on these different models. So, an example is, we have a partnership with AlzForum to maintain and update a PD models database on their site. And it really is hosting a number of commonly used Parkinson's disease rodent models, providing a timeline view of the phenotypes within the lines, and then an expanded view, basically a review of the line with all of the publications that have been using the models. So, it's a very useful resource for the community and something that we are continuing to update and then expand and add new models for folks who are interested.

**Marie:** Certainly. I think this partnership with AlzForum is really beneficial. And for listeners out there who might not have heard of AlzForum before, can you explain what it is?

**Nicole:** AlzForum is a group, and they've developed a site that really provides a lot of information, especially specifically on Alzheimer's disease, ranging from models used for Alzheimer's disease research, to research news and breakthroughs, conversations regarding that research. And I believe it was around 2015-2016 we partnered with them to kind of expand the focus to include Parkinson's disease, especially around the different model databases that they had on their site already. So, it was a very good opportunity to partner with a group who has a very interesting technology in terms of a visualization platform for the phenotypes around different models and kind of capitalize on what they've already developed to add Parkinson's disease to that focus.

**Marie:** Well, thank you for explaining that, and I know in science, time is sort of always of the essence, so, for researchers out there who might be considering using one of those models, what is the timeline from when they kind of identify what model they would like to use to when they might get it. Is this something you need to be planning way in advance of submitting your grant, or something that once the grant is received, you should put in your application to get one of these models?

**Nicole:** Yeah. So, it all depends. And I would say that's where our Sponsored Tools Program comes in. We're really trying our best to shorten those timelines so that
researchers don’t have to wait extensively and have huge delays in their studies when they’re ready to use a model. So, a lot of the models listed on those sources are already available through repositories like the Jackson Laboratory or other companies out there. And the ones that are not available and are still only in academic labs, we’re still looking at opportunities to move them to repositories so that folks don’t have to worry about those timelines. So, I would say you definitely need to plan ahead to make sure that you have the cohort of animals or cells available when you are ready to start your research program, but we’re trying our best in our Preclinical Tools team to make sure that those timelines are reduced.

Marie: Well I think that you’re doing outstanding work there with all of your collaborators, and partners, as well as the team there at The Michael J. Fox Foundation. And I’d love to talk a little bit about the Tools Consortium. I think this is an important piece of the puzzle as well. So, Nicole, can you explain what this consortium is, who is involved, and what are the goals of getting this group together to talk about what is needed in terms of tools?

Nicole: Sure. So, our Research Tools Consortium really is looking at tackling the research tools need in industry labs. So, I think there’s a common misconception that industry groups don’t have an issue with tools or models because they can make them in their own labs. And they have the money to do that, or the price of tools don’t impact them because they are pharma or biotech companies, and they’re for-profit entities but that’s really not true.

We find that industry groups are especially burdened by a lack of research tools and models in the community. And for a disease like Parkinson’s disease where the vast majority of cases are sporadic, and we don’t have a clear pathogenic link to what is happening to start the disease process, it can be a big disincentive to research and develop therapies for that disease if there are no preclinical tools and models available. So, the Preclinical Research Tools Consortium is a group of industry partners, ranging from large pharma to smaller biotechs, that are really focusing on identifying needs that are impacting industry or the community at large. There’s usually almost entire overlap there, and suggesting directions for our program to take, and nominating tools that we could focus on, and providing us with feedback and expertise and troubleshooting help if our existing projects are in need of that as well. So, this is a very important resource for the Foundation. An important consortium for us. It’s really focusing again on pre-competitive needs, and I would say, it really speaks to the collaborative nature of the industry groups in Parkinson’s disease research.

We have a number of folks, and have had a number of folks, on this consortium. Currently, there are six or seven members. And these range from groups like Biogen, and BMS, and Merck, and Lily, and Takeda, to smaller companies like
Coave so it's really a lot of insight from these field leaders in these for-profit entities that can help us decide the direction of our program and provide feedback on some of our current initiatives to increase our chances of success and make sure that we are also keeping in mind what would speed therapeutic development on the industry side.

Marie: Oh very interesting. And to give our listeners a sense of just, I guess, how it works — how often does the group meet, and how do you decide who the members will be?

Nicole: Any group that has an active therapeutic program and is an industry group or a pharma group can look to participate in this consortium. Really we meet quarterly for one hour teleconferences, and those teleconferences really focus on an overview of our current pipeline as well as MJFF bringing exciting updates on current programs and development, future directions that we're looking to get feedback on, we sometimes bring projects that need troubleshooting to see if our consortium members have any feedback for us or any suggestions for new directions to take. So, it's really a discussion setting and update-style meeting from The Fox Foundation to our consortium partners to really inform our program and keep our partners informed as well.

Marie: Certainly. And I know, Nicole, you mentioned it earlier, but I think it's worth emphasizing here that the tools that we've been talking about today, MJFF provides those both to academic nonprofit, and for-profit companies, so that's something where you are open to working with and sharing with both of these kinds of entities.

Nicole: Yeah, definitely. We on our program really don’t discriminate between whether you're at a non-profit or for-profit institution. And globally too, we want to make sure that we’re hitting the needs of the community, regardless of institutional affiliation and location.

Marie: Definitely. And I know there's a lot of work still to be done and a lot of exciting directions we can go in terms of tool development. So, do you have a sense, Nicole, of what the future directions are or perhaps the biggest areas of opportunity that The Michael J. Fox Foundation is interested in exploring?

Nicole: So, for tool development, I think our program has evolved in interesting ways. So, the program really started back in 2010 with more of a focus on sponsored tool generation and moving tools from academic labs to repositories. We shifted probably five to seven years after that to really focus on generating tools, primarily, that the community needed. And now our program has evolved into a mix of the two, marrying tool generation and the sponsored tools program to make sure we're fitting all needs for the community.
And, historically, we focused a lot on tools that are towards more priority targets in Parkinson's disease, so alpha synuclein, LRRK2, GBA, Parkin, and PINK1. And now we're kind of exploring and developing tool sets to some of the emerging and novel targets as well. So, I think in the future, moving forward, and what we're focusing on now really is also keeping in mind that our priority targets like alpha synuclein and LRRK2 don't have all of the tools that they need.

So, continuing focus there, but really expanding out to try and develop reagents for the novel and emerging targets to make sure that we can take some of the the hits we're finding from these -omic studies and large-scale patient data sets and move those to the bench so that we can better understand the biology, the target, and develop potential therapeutic mechanisms to attacking that. So, we're really looking to expand into that space in the future. So, I think that'll be interesting and hopefully field-enabling.

Marie: Certainly. I think there is a lot to look forward to. And Nicole, is there anything else that you would like to share about The Michael J. Fox Foundation's tools with listeners out there who might be interested in using them or getting involved?

Nicole: Yeah. I would say, first and foremost, please go to our Tools page on our website so you can learn more about what we have and what we do. If you don't see something there that you were hoping to see, please feel free to reach out. You can always email us at tools@michaeljfox.org. We'd love to hear from you on both feedback on our program, where you think we should be moving, if you have tools you need that you're not able to find. If you're new to Parkinson's disease research and just want to talk about the available tools and models for this condition that could help with your research program, feel free to reach out. I would say, again, one of the big rate-limiting steps for our work is really understanding and hearing the feedback from the community. So, please use us as a resource, not only for what we have already made available, but for what we could make available in the future.

Marie: I think that's wonderful, and I think everyone there at MJFF is doing amazing work. Can you share with our listeners how you see your work bringing us closer to finding a cure for Parkinson's or maybe contributing to improved therapies for people with Parkinson's today?

Nicole: Definitely. I think our program, the Preclinical Tools and Models Program, is very interesting and unique because it really accelerates Parkinson's disease across the development pipeline. So, we're focusing on tools that enable understanding of some of these novel and emerging targets, taking things that are coming out of
patient data sets and patient studies, and seeing if in a biological model or in a new system that is linked to some Parkinson's disease pathology.

So, we're really uncovering new potential pathways and targets for Parkinson's disease at the very early stages of research all the way through to some of the more clinical phases by developing high quality antibodies that can be used in biomarker development and assay development work for clinical testing. So, I would say our program is uniquely poised to support the translational pipeline really across the entire spectrum.

Marie: Phenomenal. Well, Nicole, we really appreciate you taking the time to speak with me today to share these resources with the community. So, thank you so much for joining me on the show.

Nicole: Yeah, thank you for having me.

Marie: It's been a pleasure to chat with you and listeners wonderful to have you here as well. If you want to know how The Michael J. Fox Foundation can help your research, please visit michaeljfox.org/researchresources.

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