Alexandra Magold

Good morning, Science. My name is Alexander Magold, and it's a great pleasure to talk to Professor Amanda Sferruzzi-Perri. She's from the University of Cambridge and has led her team to fascinating work on the interplay between placenta, fetus and the mother. She has not only published the impact specific environmental factors and the health status of the mother have, but she is at the forefront of a game changing research field that identifies the placenta as a target. This target can improve not only pregnancies but also the after pregnancy live consequences for the child and the mother.

Dr. Amanda Sferruzzi-Perri

Yeah, so I guess my lab works on the placenta, which is the organ that develops during pregnancy to provide all the nutrients for the fetus to grow. And we're really fascinated by how the placenta may balance the need for nutrition by the fetus versus what the mother might need to support her health and wellbeing because she needs to support the pregnancy, of course, but also support subsequent lactation. And so the placenta forms during pregnancy to connect the fetus to the mother and is therefore in touch with the environment of the mom and the fetus and trying to save both individuals at the same time.

Dr. Amanda Sferruzzi-Perri

And we know that the placenta is playing many, many vital roles. So it's responsible for transporting nutrients and oxygen from the mother to the fetus. But it also secretes signaling factors into the mother that are thought to adjust her body system so that she can support fetal nutrient supply and then support fetal growth. And so we have been looking at the role of the mother's environment in affecting the way in which the placenta forms and functions and what that might mean for fetal outcome.

Alexandra Magold

That's amazing. What surprises most people?

Dr. Amanda Sferruzzi-Perri

Well, remarkably, the placenta is a very plastic organ, so we know that the way that it functions is really determined by the environment of the mother. So what she's eating, her levels of adiposity, whether she's stressed these all affect the way in which the placenta forms and transports nutrients to the fetus and actually with sort of moderate stresses like mild undernutrition or mild levels of stress or mild oxygen deprivation, which is a model that we look at in the lab, or mild obesity, the placenta will actually adapt its function, even though the mother may not be so good at providing nutrients to the fetus and may actually transport more nutrients and oxygen to the fetus to optimize fetal growth in that prevailing environment. Whereas in the case of more severe insults like severe obesity or severe undernutrition, high levels of stress which we know are big risk factors for poor pregnancy outcome, the placenta will actually transport less nutrients to the fetus and probably contribute to the poor fetal outcomes in those pregnancy, but

probably then allowing the mom to survive, maintain her health so she can support the baby in pregnancy and in later post-natal life.

Dr. Amanda Sferruzzi-Perri

And so we're trying to understand how the placenta might sense the environment of the mother, what determines the way it responds and therefore influences fetal growth. And so the work really highlighted the importance of the mother's environment, which is a very strong, modifiable risk factor. But if we can understand what are the factors that determine the placentas response to the environmental conditions, then maybe we could target those to optimize placental support of fetal growth and optimize fetal growth as well as maternal health in the pregnancy.

Alexandra Magold

Do we have to imagine this more like a threshold, or is that the length of the insult?

Dr. Amanda Sferruzzi-Perri

It could be a combination. So we're trying to study that so we know that timing is really important in gestation. So, as you can imagine, an insult that might happen later in pregnancy when fetal growth is maximal and the ability of the mom to support that demand for nutrients and oxygen is really high. Any challenge to the mother at that point is going to have a larger effect than, say, earlier in gestation when the demand for resources by the fetus is much lower.

Dr. Amanda Sferruzzi-Perri

We also know that it's not just about the precise time in gestation, but the length of the insult, actually, sometimes a longer longer exposure to an insult might allow the pregnancy to develop in a way that it's adapted and could therefore optimize, whereas a more acute insult might be more detrimental. But it certainly depends on the the severity of the insult, the timing of the insult, the duration and how that may relate to the needs of the mother versus the fetus.

Dr. Amanda Sferruzzi-Perri

You could, of course, imagine that in early pregnancy, like I said, the fetus doesn't need much nutrients. It's actually the mom she's distributing building up her reserves so she can support fetal growth later in gestation, whereas that shift towards the fetus is in later gestation when fetal growth is much greater. So we do think that there are, though, certain thresholds. But yet again, it's environment specific, and we're actually trying to study that directly in the lab by having different severity levels of an insult and then comparing the gene and molecular pathways that are activated with a one type of level insult versus a stronger insult, if that makes sense to try and understand and so to govern the response.

Alexandra Magold

Yeah, yeah, wow, that's that's amazing. That's really great. You were awarded the Hands Sigrist Award, right?

Dr. Amanda Sferruzzi-Perri

So, I mean, the best part about this particular prize, so it is monetary, but the fantastic thing is that I can take that money to support important people in the lab to continue their career path and also the research, because our field is quite under funded compared to other disciplines like cancer biology, for example. So having the freedom to support important people that help the continuation of the research is really important. It also acknowledges our field as a really key area.

Dr. Amanda Sferruzzi-Perri

Which again, as I highlighted, doesn't receive as much attention, but is fundamentally important for the survival of our species.

Dr. Amanda Sferruzzi-Perri

I mean. Having a baby allows the passing of genetic material, and we know that if the placenta doesn't form and function properly, you can get pregnancy complications like fetal growth restriction, preeclampsia, gestational diabetes. And these conditions not only affect pregnancy, but can also lay a legacy of poor health for the mother and the child in the years after the pregnancy. So with this prize money, not only does allow us to undertake research and explore novel areas, which I can tell you about, if you like, but also it gives us the ability to network to collaborate with others, particularly in Europe and in Switzerland, where the foundation is, where I can host students in my lab and similarily I can also go to Berne to share expertise, share training, of course, within any lab, you become specialized with particular techniques and systems, and really it's the working to work with other labs that allows you to really explore fundamental principles. It can't really be done by yourself. And so this will give us the opportunity to exchange expertise models, train others, that would be hopefully also moving into research and therefore have a wider, far reaching impact. In the field, but also broadly to medical research.

Alexandra Magold

Yeah, awesome, you teased me a little bit with that, you could talk about further avenues. And so if you're up for that?

Dr. Amanda Sferruzzi-Perri

Oh, yeah. I mean, the placenta is remarkable because it has to develop and support two individuals at the same time. And in our work of looking at the response of the placenta to the mother's environment, we've we and others have identified that the placenta is not really just a passive receiver of signals. It actually

communicates needs of the fetus to the mother through its production of signaling factors like hormones. And so we're actively trying to look at what is the role and what is the identity of those signaling factors that may be remote controlling the mother.

Dr. Amanda Sferruzzi-Perri

To optimize nutrient and oxygen supply to the fetus during pregnancy, and so we've been actively trying to study this in the lab and we have techniques to modulate the way in which the placenta produces signaling factors and our unpublished. Yeah, just manipulating the placenta, leaving the mother and the fetus normal. And we're doing that in normal healthy pregnancies, but also pregnancies where we have superimposed a suboptimal unfavorable environment of the mom, like poor nutrition, obesity.

Dr. Amanda Sferruzzi-Perri

And that work has already identified to us that if the placenta doesn't produce the right amounts of these signaling factors, that does affect the body systems of the mother, like the way in which she handles the nutrients she takes in, how she uses them versus gives them up to the fetus. It affects her behavior, her food intake, her activity levels. And we know from other work also that it impacts on other things like nesting behavior to prepare her for the lactation.

Dr. Amanda Sferruzzi-Perri

And that if the placenta hormonal signaling factor production is disrupted, these changes don't occur to the right level. And that impacts on fetal nutrient supply, fetal growth and maternal health and in following up these pregnancies. This has lasting impacts on the health of the mom and the child. So we're hoping that these factors that come out, the placenta could serve as indicators of well-being, that we could therefore either intervene in a pregnancy or target the placenta in some way to try and optimize the outcome and optimize maternal and fetal health in those pregnancies.

Alexandra Magold

And so how is this underfunded?

Alexandra Magold

This is so screaming in your face, especially, I'd say, in the Western world where everybody gets older, has less kids - unbelievable!

Dr. Amanda Sferruzzi-Perri

And right, some are of advanced maternal age I mean, we know that all of those things are strong risk factors and increase the risk of pregnancy complications. I suppose the short answer, I think two components to this one is I think that people don't realize how common pregnancy complications are. It's

quite a personal thing when I speak about the work that I do. Oh, yeah, I know someone that developed diabetes in pregnancy or I had a small baby or they delivered the baby early. It's quite a personal experience and quite traumatic for the couples involved and when I speak to people, they're shocked to hear that it occurs in around one in eight women in a developed country in developing countries, as much as one in four or five.

Dr. Amanda Sferruzzi-Perri

So I think, one, it's the lack of awareness of how common these complications are and also that actually we do know very little about the placenta, how these complications arise. And also we have very little to do in terms of treatment and prevention. So I think that is a main component. Also, I think that most people think that pregnancy that the impacts of an adverse pregnancy health status just impacts on the pregnancy without thinking about the longer lasting effects.

Dr. Amanda Sferruzzi-Perri

So we know, for example, if a fetus receives poor nutrients during development, those organs within the fetus don't develop properly and they're likely not to function so well. When that baby, even if that baby is born in that baby in later life, and especially if that baby is then eating a poor diet with high sugar and high fat, they're going to have greater risk of developing obesity, type two diabetes.

Dr. Amanda Sferruzzi-Perri

So this perpetuation of disease. Also say the organs of the fetus that are responsible for giving rise to the next generation, so the ovaries of the developing fetus, which have the eggs, that will then be the subsequent generation, if those are altered, then you could imagine transgenerational effects. So I think the lack of awareness that a poor pregnancy outcome can have multiple effects on multiple generations, impacts on the funding, and then finally, I think people tend to think about treatment rather than prevention.

Dr. Amanda Sferruzzi-Perri

But in the case of a pregnancy, we have a real opportunity. Well, even pre pregnancy health, we have an opportunity to improve lifestyle health, to improve pregnancy outcome, to prevent the programming of elevated disease risk in the child that will therefore then be the parent of the next generation. And so I think that part of the lack of funding is the lack of awareness of this long term impact, but also that people may be more focused on treatment rather than prevention or that they're not aware of how things could be prevented.

Dr. Amanda Sferruzzi-Perri

I mean, I think really the the field in general was pioneered probably from the late 80s to early 90s where an epidemiologist so people that look at sort of health records and map that to the development of

diseases in years later had shown that actually babies that were born of low birth weight, which is an indicator of poor reduced nutrition, they were at greater risk of developing heart disease, type two diabetes, obesity than those babies that were born of normal weight.

Dr. Amanda Sferruzzi-Perri

And this was after adjusting for confounders like smoking socioeconomic status. And so really that paved the field for trying to understand, well, how is that how are those origins of supposedly adult onset diseases derived from a poor intrauterine environment? And then what determines that environment being the mother's environment and the placenta as a mediator of that between the mother and the fetus during gestation?

Alexandra Magold

Well, what potential? I just can't get over the fact that we're tweaking the environment for all of whatever a year or two years, something like this, for the mother, it could change the entire life, not only of the offspring, but also of of the entire family, because they have to take care of each other. Right? I mean, if we just were looking at it from a very heartless perspective and just thinking of the economic implications.

Dr. Amanda Sferruzzi-Perri

100 percent and we also know, which I probably forgot to say, is that, say, a mother develops a complication like gestational diabetes or preeclampsia. So poor glucose control or poor blood pressure control in pregnancy, those women are much more likely to develop Type two diabetes and heart disease in later motherhood. So they're sort of memories both in the mother's tissues, but also in the the fetal tissues that can lead to the perpetuation of disease with sort of lifelong societal economic impacts.

Dr. Amanda Sferruzzi-Perri

And and that's where this sort of Hans Sigrist Award is really fundamental for raising awareness of the importance of this field so that hopefully other funding agencies will also put more funds towards prevention and early life origins rather than treatment of the diseases that could have this sort of very early life start.

Alexandra Magold

Yeah, this should be a no brainer. I mean, this is so I'm just floored. Well, thank you so much.