

# GoPI3Ks



## NEWSLETTER

December 2014 Issue 1

Genetic Overgrowth PI3K Support

[www.gopi3ks.com](http://www.gopi3ks.com)

Welcome to the first newsletter for GoPI3Ks – Genetic Overgrowth PI3K Support. Our aim is to keep you informed of the current research in segmental overgrowth, interesting news articles and items of interest.



### News from the Segmental Overgrowth Study

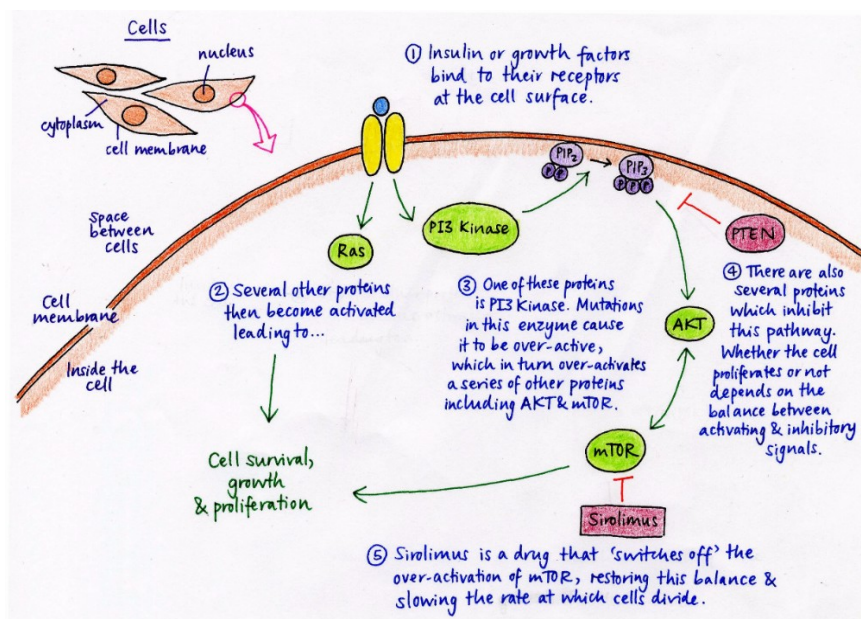
It has been a busy year in the lab and we feel real progress has been made in understanding more about the causes of segmental overgrowth. At present we are focussing on three key questions;

1. How do genetic changes in *PIK3CA* and related genes cause overgrowth?
2. What is the natural history of overgrowth?
3. Are there any treatments that will help?

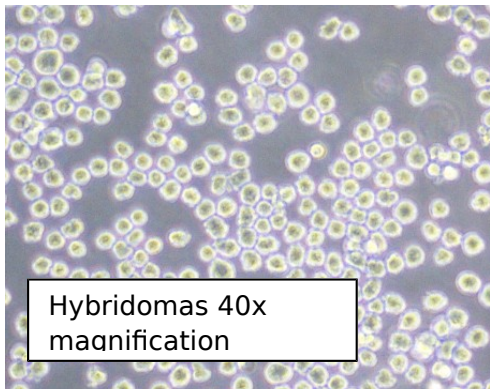
We remain extremely grateful for the contribution of all of our study participants and their families in our research, as without their help, none of this work would be possible.

#### HOW DO CHANGES IN THE GENE *PIK3CA* CAUSE OVERGROWTH?

In affected tissue from patients with segmental overgrowth, genetic changes (mutations) in the gene *PIK3CA* (also known as PI3kinase) or other



related proteins lead to over-activation of the cell machinery controlling cell growth (proliferation).



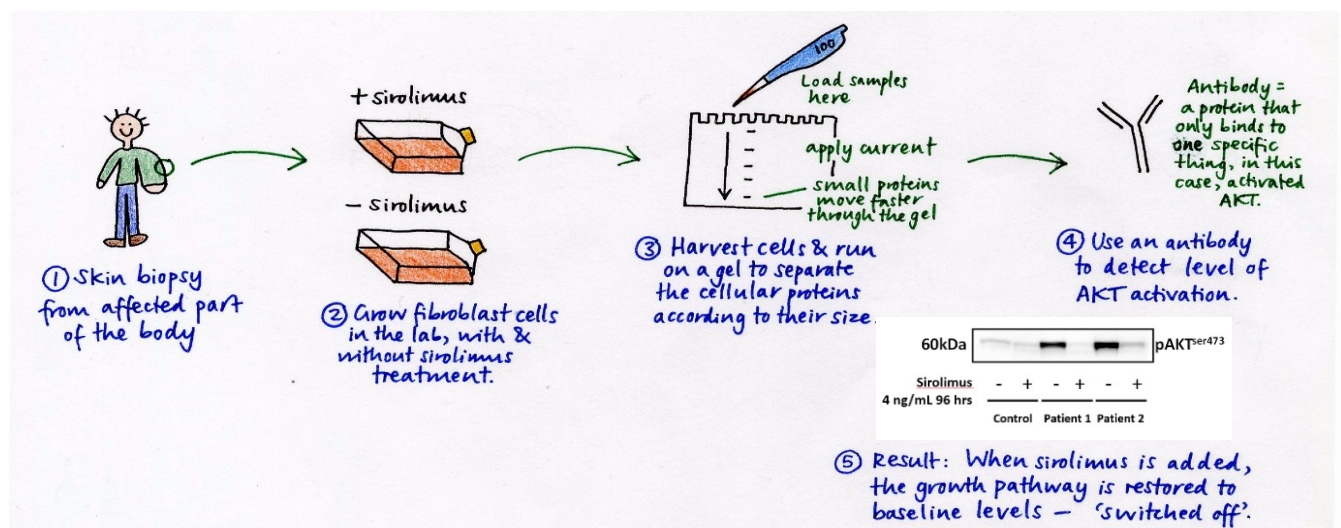
## WHAT CAN BE LEARNT ABOUT THE NATURAL HISTORY OF OVERGROWTH?

We have learnt that some people with segmental overgrowth carry on growing, whereas some stop growing when they become a young adult. Why is this? To answer this question we have made some antibodies that will detect the mutant form of the protein encoded by the gene *PIK3CA*, which will allow us to identify precisely

which cells and tissues are affected. The cells in the picture are called “hybridomas” and are like small factories, which produce the antibodies. This work will start in early 2015, and we are excited about what can be learnt here, and hope it will help us to make better predictions about how growth will progress in affected patients.

## ARE THERE ANY TREATMENTS THAT WILL HELP?

We have been testing a number of different treatments in the lab on cells grown from our study participants. We have found that several treatments are able to switch off growth signals in affected cells, and slow down growth. One of these drugs is called sirolimus (also known as rapamycin), and is currently used to treat patients with kidney transplants. From this work we think this is the first drug that should be tested in clinical trials.



## UPDATE ON CLINICAL TRIALS

The design of a clinical trial of sirolimus treatment has been finalised and the plans are currently under review by research experts and ethical

committees. We anticipate the trial will start in spring 2015 and is for anyone with a confirmed genetic change in *PIK3CA* and progressive overgrowth. The trial will involve receiving sirolimus treatment for six months with scans before and after treatment to test if the drug works. If you are interested in the clinical trial please get in touch.

For further information visit our Facebook page, website or Twitter feed.

<http://www.overgrowthstudy.medschl.cam.ac.uk/>



<https://www.facebook.com/segmental.overgrowthstudy>



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## A WORD FROM THE PRESIDENT OF GOPI3KS – MANDY SELLARS

### Taking Rapamycin/Sirolimus

With current research in to this drug and with the possibility that many more people could be taking this in the future, I wanted to pass on my experience of being the guinea pig and how taking Rapamycin has affected me.



I started taking Rapamycin in September 2012, or as I like to call it, my magic pill. When I was first told about the possibility of taking a drug that could potentially stop my overgrowth and may even shrink my affected areas, my initial reaction was, 'well what are we waiting for, let's give it a go.' I had never been given such a lifeline and couldn't wait to see what effect it may have. Yet, I did have to consider the possible side effects. The list of these is endless, from minor things such as headaches to more serious effects such as depressing the immune system. I took the logical approach of weighing up the pro's and cons to taking the medication or not taking the medication. In the end though my heart came out the winner, I didn't want to look back in years to come and think 'what if,' life can have too many of those and I wasn't willing for this to be one of those moments.

After all what did I have to lose? My life was heading in a direction that I wasn't in control of. My legs were getting heavier, I was constantly tired from mobilising around all day in my manual wheelchair. Transferring to the bed, to the shower seat etc was getting harder; the strain on my body, especially my arms was becoming more noticeable. I had to give this a go, the alternative of becoming bed bound wasn't something I wanted to face and this was my potential way out and hopefully the start of a new life.

That moment of taking the first pill was exciting but I was also full of nerves too. What if I had a bad reaction to it? What if I developed one or more of the side effects?

After some initial tests I went on my way and carried on with my life. I took the pill at the same time every day; I also started to exercise more and started to eat more healthily.



After all, there is no point in eating lots of high calorie and high saturated fat foods when you want to lose weight. My philosophy is, 'if you are going to do something, you might as well give it all you have, then you have no regrets that you didn't try harder.'

My check up's since have always been very positive, losing weight on my legs and foot, gaining muscle in my arms and even putting a little weight on my arms.

The only small side effect was a slight rise in my cholesterol; however, using a cholesterol reducing margarine spread has brought this back down again.

In total I have lost just over 4 stone/26.3 kilos so far and counting.

It still seems like a dream at times, how a little pill can make such a difference to one person's life is mind blowing. I have so much to thank Dr Parker and Dr Semple for, as they have saved my life.

**By Mandy Sellars**

Hopefully as the newsletter grows we can share information to places, companies, support groups etc that are helpful for people with disabilities and those individuals like us. So if anyone has any links that would be useful please email me at: [funnypaws2004@hotmail.com](mailto:funnypaws2004@hotmail.com) and I will pop them in the next newsletter.

Here are a few that I have come across recently

I know that for many of us living with an overgrowth condition that getting clothes can be a logistic nightmare. I have found this company in Yorkshire in the UK who specialise in altering and making clothes especially for those who are a different shape:

<http://www.clothingsolutions.org.uk/>



An extremely accessible self-catering cottage

in the scenic village of Oban in Scotland:

<http://www.portselma.co.uk/index.html>



Two useful sites to understand the changes in the benefit system in the UK: <http://www.entitledto.co.uk> and <http://www.welfarerights.net/home.php>





Here are a few articles that I found thought provoking and interesting:

## A Point of View: Happiness and disability



Surveys reveal that people with disabilities consistently report a good quality of life, says Tom Shakespeare. So why is it often assumed they are unhappy?



**Disability is a matter  
of perception. If you  
can do just one thing  
well, you're needed  
by someone.**

**Martina Navratilova**



Have you ever thought to yourself: "I'd rather be dead than disabled?" It's not an

unusual reflection. Disability, in everyday thought, is associated with failure, with dependency and with not being able to do things. We feel sorry for disabled people, because we imagine it must be miserable to be disabled.

But in fact we're wrong. It's sometimes called the "disability paradox". Surveys reveal people with disabilities consistently report a quality of life as good as, or sometimes even better than, that of non-disabled people.

Impairment usually makes little difference to quality of life. [Research shows](#), for example, that overall levels of life satisfaction for people with spinal cord injury are not affected by their physical ability.

Even the clinical facts of whether their spinal lesion is high or low, complete or incomplete - all aspects that affect functioning - don't seem to make much difference. Human flourishing is possible even if you lack a major sense, like sight, or you can't walk, or you're totally physically dependent on others.

So what's going on?

If you think about it for a moment, you realise that people born with an impairment have nothing to which they can compare their current existence. Someone lacking hearing or sight has never experienced music or birdsong, visual art or a sublime landscape. Someone with an intellectual disability may not consider themselves different at all. Someone like me, born with restricted growth, has always been that way. Even if life is sometimes hard, we are used to being the way we are.

For people who become disabled, there's a typical trajectory. I can say this from personal experience, having become paralysed in 2008. Immediately after the onset of injury or disease, one can feel profoundly depressed, and even contemplate suicide. Yet after a period of time, people adapt to their new situation, re-evaluate their attitude to the disability, and start making the most of it. Sometimes, they are driven to greater achievements than before. Remember those amazing Paralympic athletes...

Maybe you are sceptical about the subjective nature of quality-of-life data. Bioethicists sometimes describe these self-reports in terms of the "happy slave" concept, in other words, people think they are happy because they do not know any better. Perhaps these cheerful people with disabilities are deluding themselves. Or, perhaps they are fooling others. Maybe in private they admit to misery, while in public they put on a brave face. Either way, it's said these folk must be in some kind of denial.

But these explanations are patronising, not to say insulting. More importantly, they're wrong. Research in a field called hedonic psychology has supported disabled people's self-reports of good quality of life. Scientists such as Daniel Gilbert have done very thorough testing of what people say and how they think. They've come up with the concept of hedonic adaptation - which refers to the way in which after trauma, quality of life eventually returns to approximately what it was before the trauma struck. Amazing, eh? Unfortunately this also happens in reverse - so, if you are lucky enough to win the lottery, you'll feel like £10m for a year or two, but then you'll go back to being as miserable or cheerful as you were before your stroke of luck.

So if these self-reports are true, we will need to find better ways of understanding the disability paradox.

To start with, we can offer more nuanced accounts of the psychological processes

that go on in the mind of a person with disability. Adaptation means finding another way to do something. For example, the paralysed person might wheel, rather than walk, to places. Coping is when people gradually re-define their expectations about functioning. They decide that a stroll of half a mile is fine, whereas previously they would only have been content with a 10-mile ramble. Accommodation is when someone learns to value other things - they decide that rather than going for walks in the country with friends, it's far more important to be able to go to great restaurants with them. This teaches us an important lesson - human beings are capable of adapting to almost any situation, finding satisfaction in the smaller things they can achieve, and deriving happiness from their relationships with family and friends, even in the absence of other triumphs.

Our appraisal of life with impairment may have less to do with reality than with fear and ignorance and prejudice. We wrongly assume that difficulties for people result in misery for people.



mar Sy and Francois Cluzet in a scene from the film Les Intouchables, 2011

Even to the extent that impairments do entail suffering and limitation, other factors in life can more than compensate for them. Take the recent French box office sensation Les Intouchables, in which the protagonist, Philippe has tetraplegia, but despite this, he is able to have a good quality of life because he has money. Even people who aren't lucky enough to be wealthy Parisian aristocrats can enjoy the benefits of friendship or culture,

despite the restrictions that impairment places on them. By contrast, it is plain to see that someone can have a fully functioning body or mind and yet lack the social networks or the personality necessary for living a happy and fulfilled existence.

This highlights the importance of the environment in determining the happiness of disabled people. As in most areas of life, it's structural factors that make the real difference. Participation, not impairment is key. Do access barriers stop you going to school with your friends? Do you have a job? Does society meet the extra costs of having an impairment through a welfare system which is fair and non-stigmatising? Do you face hostility and hate crime? Unfortunately, in most of these respects the situation for disabled people has been getting worse, not better, in recent years. According to the Centre for Welfare Reform, this government's spending cuts have had a hugely disproportionate impact on the lives of disabled people in poverty.



In arguing that social barriers are more of a problem than the impairment itself, I am not suggesting that fear is completely irrational. For a start, disability is very diverse in ways that mean we have to soften the claim that "disability is no tragedy". Some illnesses and impairments undoubtedly involve greater degrees of misery or suffering than the average human should have to endure. I'm thinking of depression, for example, which biologist

Lewis Wolpert memorably labelled "malignant sadness". There are some nasty and painful degenerative diseases. Impairments that involve considerable pain, whether physical or mental, are obviously less compatible with a good quality of life.

It's also true that in general, disabled people usually have fewer choices than non-disabled people. Most societies still have limited accessibility. Even in a barrier-free world, the disabled person is more likely to rely on mechanical devices that periodically malfunction, rendering the individual excluded or dependent. I have been stranded thanks to a flat tyre on my wheelchair or a broken lift numerous times. Most disabled people become inured to the frustrations of inaccessibility or breakdown, but it certainly makes life less predictable and less free than it is for the non-disabled.

But my point is that while disability is not simply an irrelevant difference, like the colour of your skin, neither need it be a tragedy.

And remember: Mere existence entails problems. Hamlet, listing reasons why death is to be preferred, highlights "the thousand natural shocks that flesh is heir to". To be born is to be vulnerable, to fall prey to disease and suffering, and ultimately to die. Sometimes, the part of life that is difficult brings other benefits, such as a sense of perspective or true value that people who lead easier lives can miss out on. If we always remembered this, perhaps we would turn out to be more accepting of disability and less prejudiced against disabled people.

Article by BBC 1/6/14

<http://www.bbc.co.uk/news/magazine-27554754>



# Lesser-known things about being a wheelchair user

By Ouch team BBC News



While every wheelchair user is unique, whether self-propelled, powered or pushed by someone else, there are aspects of life on wheels that they can all identify with. Below are five things that wheelchair users know but others perhaps don't.

## It's a miracle!

If you've ever seen someone stand up from a wheelchair and walk, don't assume you've just witnessed a miracle or a Blue Badge fraudster.

It's not uncommon for people who can move their legs to use wheels to get around some or all of the time. There are a multitude of reasons for this, pain, fatigue or muscle weakness to name just three.

Twenty-one-year-old part-time wheelchair user Bethan Griffith-Salter has been called a fraud on numerous occasions for folding away her wheelchair and walking. She says she feels angry that she is expected to give details of her medical condition to strangers who challenge her about having a chair when she is able to walk.

"The biggest thing to remember is this: if you do not know the person," she says, "then why they use a wheelchair is none of your business."

## Bums in faces

Unless they own a whizzy model that can elevate them, the face of a wheelchair user is at a different level to those of people who are upright. For ex wheelchair athlete Baroness Tanni Grey-Thompson, this is most noticeable when travelling "at crotch level on the tube" and "having someone's bottom in my face that wobbles about when the train moves".

Griffith-Salter says being lower-down makes her feel claustrophobic when she can't get through a crowd or see in front of her. She says "sitting" in busy places can be dangerous. "I have been hit on the head many times by shopping bags ... and people have come straight at me with cigarettes."



Advice: Never push without asking permission first

## Wheelchair etiquette

"I was in canary wharf," says Baroness Grey-Thompson, "when someone came up behind me and asked me if I needed a push. I said no, and then they pushed me anyway. I was really shocked that they didn't listen to my answer."

The general consensus is that one should never push a wheelchair without express permission from the owner, even if they aren't currently sitting in it.

Other points of etiquette include not walking behind the wheelchair user, and never leaning on the back of someone's chair or using it as a trolley. Griffiths-Salter says you should think of a wheelchair "as part of the user's body".

### "Decent wheelchairs are expensive"



My advice to other disabled people would be, concentrate on things your disability doesn't prevent you doing well, and don't regret the things it interferes with. Don't be disabled in spirit as well as physically.

Stephen Hawking



Wheelchairs sold in big retail stores for under £100 tend to be one size fits all. They might work fine for occasional days out with Grandma but for those who use theirs regularly, only a bespoke wheelchair will do. These are a lot more expensive, often running into the thousands. For example, at the top end, Paralympic-grade sports wheelchairs can cost as much as £50,000.

Dave Hawkins runs Cyclone Mobility, has a spinal injury and uses a wheelchair himself. He says that the key considerations when choosing a chair are "weight, then functionality, and then aesthetics". The lightest wheelchairs available nowadays are made from carbon fibre.

Hawkins says there are critical health considerations when customising a

wheelchair for a client. The position of the footplates, seating angle and backrest position, determine posture and whether you get pressure sores, a common and dangerous problem. "Shoulders rounded and neck going forward can result in massive costs for the NHS," he says.

Aesthetically, he says that women and men want slightly different things from their wheelchairs.

"This is a generalisation but I find that ladies want something more colourful and en vogue, like anodised purple sections on it to match their nail polish." He says men tend to treat customising a chair a bit more like they would a car, choosing the most up to date materials and engineering for an improved performance.

### The joke's on you

"If you think you've just come up with the world's funniest gag about wheelchairs, keep it to yourself. I can assure you we've heard them all and we only smile pitifully to make you feel less awkward," says Shannon Murray.

The wheelchair-using model and presenter says the gags are so poor and so regular that she can't remember them word for word, but that they always run along similar lines.

"If I'm in a bar and I'm holding a drink there is usually someone who makes a joke about drink driving. I used to use a chair made by 'Quickie' so that would lead to hilarious comments about jumping on board for a quickie or taking me for a spin around the block." Speeding jokes, she says, are also common.

# Disability day: What are you doing?

By Emma Tracey BBC News, Ouch 11:03  
UK time, Wednesday, 03 December 2014



People in India took part in a rally to mark the day last year

People over the world are marking the International Day of Persons with Disabilities (IDPD) and have been getting in touch to tell us what they are doing.

All around the world, people are encouraged to get together to celebrate disability identity. It has been observed annually by the United Nations since 1992. It promotes disability rights and the benefits of integrating disabled people into all aspects of life.

Events in the UK tend to consist of performances by disabled artists and live discussion forums. This year, Liverpool's DaDaFest are running their inaugural international congress on how disability arts has affected social change. The Central Library Manchester will give disabled people hands-on access to the books and artefacts on display in a First World War exhibition. And in Cardiff, Disability Wales are running an event to help shape their new manifesto.

So far, most disabled people who've contacted us weren't aware it was happening.

James West, who has MS, obviously doesn't think it's a very special day, lined up for him is: "dragging myself out of bed and going to work, as I do every day". Along similar lines: "I will be spending another day on public transport being kicked about & having to ask for a seat from oblivious folk", tweets Penny Rabiger.

And @dorsetcharlie isn't impressed by the name of the day. She tweeted: 'International Day of Persons with Disabilities' Really, that's the best name they could come up with?! #PCMadness

@catobellingsen is at a conference in Oslo

But @catobellingsen got in touch to tell us he is attending a conference in Oslo on growing up with a disability in Norway, where the minister for social inclusion Solveig Horne is speaking.

And @iainmassingham tweeted to say he is spending the day "showing thanks that I am part of the amazing disability football club @AFCMasters #football4all". As the day rolls on, we'll be tracking what people are doing.



This year's theme as set by the UN is - Sustainable Development: The Promise of Technology.

Though the UN calls it IDPD, it seems to also go by other names and acronyms depending on language preference. The Department for Work and Pensions in the UK are referring to it as IDDP and many have inserted a W for 'with' as in IDPWD.

Sometimes, though, the IDPD bush telegraph goes quiet and it feels like the day goes by without much fuss or fanfare. <http://www.bbc.co.uk/news/blogs/ouch/>

**So what do you think?  
Do we need a Disability Day?**

**Would you go to an event  
if it was in your area?**

**Or should we just celebrate  
who we are every day?**





Life is like  
photography, we use  
the negatives to  
develop.

(author unknown)



**“Finally we would  
like to wish you a  
very merry  
Christmas and a  
happy and healthy  
new year”**



Thank you for reading our first newsletter, if anyone would like to contribute to the next one,  
please email me (Mandy) at: [funnypaws2004@hotmail.com](mailto:funnypaws2004@hotmail.com)

