

AUDIO INTERVIEW TRANSCRIPT

## Blackburn, Tom: transcript of an audio interview (22-Feb-2016)

**Interviewer:** Tilli Tansey

**Transcriber:** Debra Gee

**Editors:** Tilli Tansey, Apostolos Zarros

**Date of publication:** 30-Jun-2016

**Date and place of interview:** 22-Feb-2016; Queen Mary University of London

**Publisher:** Queen Mary University of London

**Collection:** History of Modern Biomedicine Interviews (Digital Collection)

**Reference:** e2016045

**Number of pages:** 24

**DOI:** 10.17636/01013141

**Acknowledgments:** The project management of Mr Adam Wilkinson and the technical support of Mr Alan Yabsley are gratefully acknowledged. The History of Modern Biomedicine Research Group is funded by the Wellcome Trust, which is a registered charity (no. 210183). The current interview has been funded by the Wellcome Trust Strategic Award entitled “Makers of modern biomedicine: testimonies and legacy” (2012-2017; awarded to Professor Tilli Tansey).

---

**Citation:** Tansey E M (intvr); Tansey E M, Zarros A (eds) (2016) *Blackburn, Tom: transcript of an audio interview (22-Feb-2016)*. History of Modern Biomedicine Interviews (Digital Collection), item e2016045. London: Queen Mary University of London.

---

**Note:** Audio interviews are conducted following standard oral history methodology, and have received ethical approval (reference QMREC 0642). Related material has been deposited in the Wellcome Library.

© The Trustee of the Wellcome Trust, London, 2016

## Blackburn, Tom: transcript of an audio interview (22-Feb-2016)\*

**Biography:** Dr Tom Blackburn CBiol MIBiol MPhil PhD DSc HonFBPhS (b. 1949) received his degrees from Nottingham and Manchester Universities. He has held C-level executive and senior management positions at ICI Pharmaceuticals plc, Beecham Pharmaceuticals plc and SmithKline Beecham in the UK, and with two biotech companies in the US, Synaptic Pharmaceutical Corporation and Helicon Therapeutics Inc. He has led companies, departments, and project teams that identified and developed novel therapeutics, including several serotonin receptor subtype antagonists (5-HT<sub>2A</sub>, 5-HT<sub>2B</sub>, 5-HT<sub>2C</sub> and 5-HT<sub>3</sub>), galanin receptor 3 antagonist and the selective serotonin reuptake inhibitor (SSRI) antidepressant, Seroxat/Paxil. His passion, based on an extensive knowledge of pre-clinical/clinical drug development and marketing, helps to define strategies and positioning of pharmaceutical products for biotech startup companies. He is currently Founder and CEO of TPBioVentures LLC, a 'virtual' drug development and consultancy company in the US and UK. He has authored over 100 peer reviewed scientific papers, review articles and book chapters and is an inventor on 22 patents. He is President Emeritus of the British Pharmacological Society and a Member of the American College of Neuropsychopharmacology. He is also a Non-Executive Director for Motac Neuroscience Ltd., a neuroscience biotechnology company specializing in Parkinson's disease and cognitive and neurodegenerative disorders.

---

**TT:** Tilli Tansey

TB: Tom Blackburn

-----

**TT:** Tom, to begin with, can we just go through your background, when and where you were born, what your family circumstances were, and what you liked at school, how you got on at school, and how you got interested in science?

TB: All right. Well, from the accent, I was born in Liverpool, where my education was somewhat compromised; I, like many children at the time, was what they call a 'latchkey kid'. I have two younger sisters and my time in junior/senior school meant going home after school while my mother went out to work. So I couldn't really do all the after school activities I wanted to do, whether they were academic pursuits, athletics, football training or whatever. I really wanted to do well at school, but also I wasn't particularly good at certain subjects; maths was one of the problems. I didn't pass my 11 Plus but did pass my 13 Plus exam. English was a bit of a problem too, because I had a stammer, which didn't really help standing up in class reading poetry and being laughed at! But, all that being said, I had a fascination with history, geography and biology. I used to help Mr Harold, who was the Biology teacher, look after the greenhouse plants and the animals. I won the 1965 Prefect's prize and my chosen book was entitled *Science, Science, Science*, by Russell Hamilton.

I've always been fascinated with science, history and geography, which were my favourite subjects. I left school with a few O levels, and I got my first job at 16 at Evans Medical in Speke, Liverpool in 1965, where

---

\* Interview conducted by Professor Tilli Tansey, for the History of Modern Biomedicine Research Group, 22 February 2016, in the School of History, Queen Mary University of London. Transcribed by Mrs Debra Gee, and edited by Professor Tilli Tansey and Dr Apostolos Zarros.

I worked on infectious bronchitis vaccine for hens, because once hens caught bronchitis, the egg production went down. So we were handling thousands and thousands of eggs, injecting with an attenuated virus and incubating the eggs and taking off the vaccine a week later. There was also a smallpox vaccine unit, again using lots of eggs. I stayed there for about a year, when a friend of mine, who eventually was my best man, told of a job in the Physiology Department at Liverpool University. I went along and got the job as a laboratory technician. During this time I'd been going to night school to finish off my A levels. I finally ended up with chemistry, biology and physics, and later I obtained a City & Guilds qualification, Advanced Laboratory Technician's qualification in Physiology and Pharmacology Techniques. At the time, I was passionate to keep on driving myself forward, wanting to educate myself in science.

At Liverpool University, I worked for Professor R A Gregory, famous for studying gastrointestinal secretion and the isolation of the stomach hormone gastrin. I did a lot of Heidenhain pouch work, where you injected histamine and looked at the gastric acid secretion in dogs. And, to earn extra money to finance my studies, I used to go in on Saturday and Sunday morning to help clean out the dog kennels. After, I had completed my City & Guilds qualifications, between 1966-1968, I then wanted to go on to do a Higher National Certificate in Biology/Microbiology. However, the university wouldn't allow me day-release another qualification. So towards the end of the 60s, I saw a job that I was very interested in at ICI Pharmaceuticals plc. My mother had worked at the Mond Division on armaments, filling shells during the war, and I'll come back to my mother again later on. I was successful in getting an interview in 1969. I remember I'd been playing football that weekend and I had a very bad ankle injury. I travelled up to Manchester on a bus on the Sunday and then down to Macclesfield for a job interview on the Monday. I hobbled up the driveway of ICI Pharmaceuticals on the beautiful Alderley Park site. And, I knew then this was the place for me. I was interviewed by Dr Mike Barrett and I got a job in Dr Dave Greenwood's and Dr Brian Leonard lab in the CNS [central nervous system] group.

**TT: By this stage you are a junior technician?**

TB: I was a senior lab technician and I was later promoted to an Experimental Officer, not long after. That must have been about 1975.

**TT: And you said, it sounds a bit daunting, you went into ICI and you're setting up all these assays. Presumably that is because of stuff you'd learnt in Liverpool with Gregory? Was Hilda Tracy there at the time?**

TB: Yes, Dr Hilda Tracy was in the lab then, she was lovely. Let's just step back a bit and talk about that period. I worked for R A Gregory, who was a tough taskmaster. I learnt all sorts of lab skills, handling data and many experimental techniques. I was well schooled by R A Gregory. He was extremely demanding, but a brilliant scientist. He always used to have these big blocks of chocolate in his desk draw and I think only once in the three or four years did I get a piece of chocolate. However, Hilda used to sneak me a piece or two occasionally [laughs].

**TT: So what was the purpose of the chocolate, was it to reward good boys and good girls?**

TB: No, it was his energy source. He'd run up and down the spiral staircase, from one floor to the other in the physiology building, where he had his experiments. He used to pound up and down them every day and weekends. Sadly, he passed away, cancer, in 1990, just after I left ICI. I also remember it was the first time I met Sir James (Jimmy) Black when he visited Gregory's lab, when I was there in the 60s.

**TT: Sir James Black visited the Liverpool physiology lab?**

TB: Yes, as we know, he was very interested in gastric secretion, and later went on to discover the histamine (H<sub>2</sub>) receptor antagonist, cimetidine (Tagamet®). So those times with R A Gregory taught me a lot about designing experiments, working in a lab, and I also often helped with the surgical operations. He taught me a lot about drugs, dose response curves and anaesthetics, various experimental procedures.

**TT: So you probably had better training than most postgraduates by the time you went to ICI?**

TB: Yes, I think so. Towards the end of my time in Liverpool, I was getting restless to further my education. I helped out in the teaching labs. There was one time with R A Gregory, that I blew it one day when I was setting up an experiment for him, and I said 'Can I be moved?' I was moved into the physiology teaching labs for over a year. I was setting up all the physiological experiments for graduate students, such as the Haldane respiratory apparatus, and all the experimental frog work; gastrocnemius muscle twitch response and frog heart studies etc. and smoking the kymograph drums to record the experiments on lever pens! I was setting up physiological experiments for medics, dentists, BScs and vets. I must admit, of all students the best practical people by far were the vets. And, the nicest people. That may sound a generalisation, but certainly the vets and the BSc-students, were very good students. I think that really covers my time in Liverpool. It was a great time to be in the city during the Mersey Beat in the 60s. However, I felt I needed to move on in my career and continue my science education. I'd always had this dream of becoming a doctor, and I would have loved to go into medicine or veterinary medicine.

The ICI days were great days too. This was in the days of Dr Garnet Davey, who was head of the site R&D, and Jimmy Black had just left. So there was a tremendous buzz about the place with regard to drug development. In the labs near me where the  $\beta$ -blocker heart drug propranolol (Inderal®) and tamoxifen (Nolvadex®) for developed for breast cancer, were developed. We had a pharmacologist called Dr James Raventos, who was the one of the scientists along with C W Suckling who developed halothane, and further along the corridor from me was Dr Ian Glen, a vet. Ian had developed propofol (Diprivan®). I did some of early CNS pre-clinical work on propofol. But my main job at the time with Dave Greenwood was developing *in vivo* assays and biochemical assays to look at anti-depressant anxiolytic-like activity in animals. We had a lot of fun in that lab in those days, teasing Brian Leonard. Brian, was one of those pipe-smoking, academic type. We did all kinds of things like drop rat droppings in his pipe and dry ice in his coffee, other various daft things. One day we had the BBC's *Horizon* team who came in to discuss the brain, neurochemistry etc., and we were working on rats and mice at the time, where we were taking the brain out, after drug treatment, putting it on dry ice, freezing the brain and then doing several biochemical assays on them. And, I'll never forget the time when Brian was looking at the camera and he then accidentally flicked a brain out on to the floor and he was following it trying to get it back on the spatula, which caused great amusement. So they were really fun times, full of good science, but hard work holding down a full-time job and part-time further education. This was 1970s, I'd just turned 21, I'd finished my Higher National Certificate [HNC] at Liverpool and I wanted to go on and do a degree course MIBiol [Member of the Institute of Biology] in Pharmacology.

I'd passed my HNC in Applied Biology/Microbiology, and I went on to Stockport College and did a MIBiol. That was a three years course in Pharmacology. The final exam was a viva and I had just broken my nose playing football, and had a very bad allergy when it came to take the oral exam. I was on anti-histamines and felt like a zombie. Dr Christine Bebbington from Stockport College and I went down for the exam with Professors Ginsberg and Goldberg at Chelsea College. I was examined and fortunately passed my MIBiol. So I got my MIBiol and this must have been about 1976. I'd married my lovely wife Jacqui in 1972, so I was studying for the next three years for my MIBiol on the dining room table after work. Thankfully, I have a very understanding and supportive wife... Our daughters came along in 1975 and 1977. And, by this time I'd finished my MIBiol and asked ICI, 'Could I do an MPhil course?' They were very good with me at ICI, Drs Barry Cox and Mike Turnbull sponsored me to go on the MPhil CNA [Council for National Academic Awards] course at Nottingham University. That was with Professor Charles Marsden on my life-long passion, 5-HT [5-hydroxytryptamine; serotonin] receptor subtypes.

**TT: You were in Alderley Edge and also studying at Nottingham?**

TB: Yes, I was in Alderley Park and Nottingham doing most of the practical work for the external degree. A busy time, bringing up a young family, doing a full-time job and then studying all hours for an MPhil. ICI management were very good to me and were keen on getting people internally to do PhDs. However, there

were one or two people who hadn't finished in three years allotted and which put me back a few years in the line for external PhD, and I think I could have been one of the last ones to go through this internal scheme. So I eventually gained my MPhil after being examined on my thesis by Professors Richard Green, Gerald Curzon and Charles Marsden, at ICI, and Richard Green will tell you the story of how I wined and dined them, and that was the only way I got the qualification!

**TT:** Let's have it on record. You bribed your way to an MPhil [laughs]?

TB: Well, not really, because friend and colleague at ICI was the restaurant manager and the restaurants at ICI Alderley Park were some of the best restaurants in Cheshire. The manager, Trevor Stone had trained at the Savoy and he was my centre half in the ICI football team. I had to drop him a couple of times because he was just too big and couldn't move very quickly. So when I used to go along to get my lunch the kind ladies used to put all the chips or food on my plate, and he'd come along afterwards and scrape some of the chips back off and give me a smaller portion - if I'd dropped him that week. But getting back to Richard and Charles. Charles was brilliant. Charles is one of my all-time heroes. Richard and Gerald gave me a tough time actually and in my thesis I'd developed a number of models, for my MPhil. People have said since, that it was like two or three PhDs, because it wasn't just one *in vivo* model I'd developed to characterise 5-HT receptor subtype, there were three or four *in vivo* models.

**TT:** Can you say a little bit more about what you did at ICI?

TB: Yes. So this was the time I was working with Dave Greenwood trying to identify new novel anti-depressants. We'd identified and were developing Vivalan® (viloxazine); viloxazine was a selective noradrenaline reuptake inhibitor and 5-HT releaser. So we're talking about the late 1970s now. Unfortunately, one of the side effects was that it caused nausea and emesis in about 25% of the population, and the marketing boys weren't very appreciative of this side effect as it was compromising efficacy and compliance. It was during this time, in 1979, Peroutka and Snyder published a *Nature* paper on S<sub>1</sub> and S<sub>2</sub> 5-HT receptors subtypes, and we were particularly interested in 5-HT at that time in the lab. I was also working on the isomers of propranolol, because we knew propranolol may have some 5-HT binding affinity. As it was widely reported in those days for its 'anti-anxiety-like' activity by snooker players, jockeys and for public speaking, that may be related to anxiolytic-like activity. So I worked on and developed a number of *in vivo* and *in vitro* models to look at this activity. I developed fenfluramine hyperthermia model; basically, fenfluramine is a 5-HT releasing agent that can increase body temperature, which I used to quantify and determine the potency of novel 5-HT agents. There had been some work in the States, by Frey using this anti-obesity drug (Ponderx®). I developed this model to test for 5-HT antagonists, as we knew in those days the so-called serotonin [5-HT] S<sub>1</sub>, S<sub>2</sub> receptors the former being sensitive to 5-HT, the latter to spiperone, and the dopamine antagonist. It was the S<sub>2</sub> activity that was later to be found to be the 5-HT<sub>2A</sub> receptor, and the one I subsequently worked on and developed for the ICI compounds.

So using this 5-HT<sub>2A</sub> (S<sub>2</sub>) receptor *in vivo* model, I basically measured the temperature of the animals pre-treated with 5-HT<sub>2A</sub> antagonists, and then given a standard dose of fenfluramine to induce the hyperthermic effect. And, using a series of classical 5-HT antagonists at the time, I produced beautiful dose response curves to these mixed 5-HT/dopamine antagonists. At the time, the medicinal chemists at ICI started to synthesize novel 5-HT antagonists to test in this and in other 5-HT models I developed. This was in Dr Craig Thornburg's chemistry section, with Drs Bob Pearce and Dave LeCount. They synthesized a number of quinolone-like compounds, which were showing greater selectivity for the S<sub>2</sub> receptor subtype, which later became the known as 5-HT<sub>2A</sub> receptor. We showed some nice selectivity in the fenfluramine hyperthermia test. Another test I developed, was the rat wet-dog shake test, which was essentially giving serotonin intraventricularly to rats in which the 5-HT system had been depleted with the neurotoxin 5,7-DHT [5,7-dihydroxytryptamine]. So you get a very exaggerated wet dog shake effect, and again you could use the selective 5-HT antagonists to block this effect. Both these *in vivo* models were sensitive to 5-HT<sub>2A</sub> antagonists. And, all these 5-HT tests, I fully automated for data collection using a Commodore 64 computer in those days.

But my all-time favourite *in vivo* model I'd developed was a 5-HT-induced rat rotational model, which was based on the 6-hydroxydopamine rotational model of Ungerstedt in Sweden. Using the neurotoxin 5,7-DHT I selectively lesioned the 5-HT cell bodies in the dorsal raphe nucleus, unilaterally. I developed a similar model to the dopamine model in that direct acting 5-HT agonists produced contralateral turning, due to supersensitive 5-HT receptors and the indirect acting/releasing 5-HT agonists, such as fenfluramine, produced ipsilateral turning behaviour. So I was able then to test these compounds in that model. But, to my surprise, what we were seeing was not a 5-HT<sub>2A</sub>-like effect, it appears to be a 5-HT<sub>1</sub>-like effect. So this was very interesting because I did a lot of research then around the 5-HT area to find agonists that showed this selectivity. And one of them was 8-hydroxy-DPAT [8-OH-DPAT], which eventually we came to know as a 5-HT<sub>1A</sub> agonist. Bob Pearce in the chemistry labs was the one to synthesize some of this for me, and in those days you worked with chemists very closely, as I'm sure you do today, because if you wanted a tool, pharmacological tool, they would make it for you and do it very quickly.

**TT:** You've talked about synthesis of quinolines and other things. Would you go next door to the guy in the chemistry lab and say, 'I've got this, it looks very interesting;' you had not only intellectual freedom, but also the operational freedom to go and do that?

TB: Yes, I went upstairs to them and we worked together on identify new pharmacological tools. A bit like the way Jimmy Black worked with his chemists. They were very much part of a team in understanding the biology, just as much as you understood the biology. They got you to understand the chemistry just as much as them, and so that was one of the best relationships with chemists I had in my ICI days. From this work, two compounds out of quite a number of compounds, ICI 169369 and ICI 170809, were identified as development candidates. We called them '5-HT<sub>2A</sub> antagonists' then, because various publications had started to come out from other pharmaceutical companies and academic groups, the Janssen group for example. With other selective 5-HT compounds, I started to work out and build up the compound data bank of 5-HT receptor subtypes and selective compounds. By this time I was an Experimental Officer, but I'd become laboratory head for all the CNS testing at ICI. So I would get compounds from all over the place in ICI to test, whether it is paraquat from the agricultural side or paint constituents. I would also profile all of the therapeutic area development compounds that were going in for clinical testing, so I learnt a lot about drug development from sitting in on therapeutic teams, and also various other compounds and drugs in the organisation.

Getting back to the MPhil. I put my MPhil together with these different tests, and thankfully I got it. And, the next goal was the PhD.

**TT:** For your MPhil, did you get support from ICI, like day release or something like that?

TB: Yes, I did get a lot support from ICI management with regard to time off in Nottingham. But, like my PhD latter, a lot of it was my holidays, which didn't always go terribly well with my wife and family. So I used to take time off for a week or so, to finish off experiments or at weekends.

**TT:** At ICI were you allowed to be doing experiments that contributed to your MPhil?

TB: Yes. They were very gracious in that, and were a great organisation to work for, we had managers like Dr Brian Newbould, who was site head then and Drs Desmond Fitzgerald and James Conway, who were very supportive and were my departmental head then. They were also very supportive in the sense, with some of the 5-HT tests I was developing. As one of things in life is I always challenge the dogma in science or whatever. And, this got me into a couple of situations where I was going against current research with my data. It wasn't corresponding to what others were saying. The likes James Conway could see where my data was taking me, and basically I got a lot of support from senior management.

**TT:** In our 5-HT Witness Seminars you actually say, 'Data trumps everything.'

TB: Yes. Robust data...

**TT:** That's an interesting period, the 70s, I've done a lot of interviews with technical staff, and that's the period when people are beginning to invest in technical staff and think, 'Hang on, these guys really know what they're doing.' They support them. Were you unusual? Were there many people that ICI were supporting to do their qualifications?

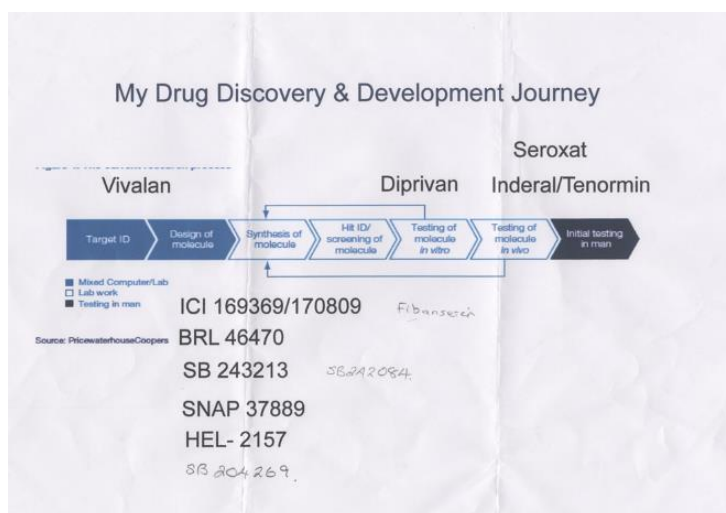
**TB:** Yes, there were one or two who went on and stayed with the organisation and achieved very high positions. And, a number of them had come through MIBiol at Stockport College, which was a very good course. That really laid the foundation for me in pharmacology to go onto the MPhil, my PhD, and then DSc.

**TT:** So you get your MPhil. That was published in a series of papers. It sounds amazing, these three different models. And you continue with Charles to do a PhD, or was it something else?

**TB:** No, I didn't because there's always management changes, and people coming in, and the focus of the organisation changed. So Dr Mike Rance came in as CNS Section Head, Dr Barry Cox, who was my one of my life mentors and an extremely important person in that 5-HT period, he came in from Manchester University in the late 70s. In developing some of these 5-HT models, I used to bounce ideas off Barry. Barry used to bounce ideas back to me, and so on during that period. Barry was very influential and also in bringing me into the loop with people like Charles Marsden. David Greenwood had moved off into clinical pharmacology by this time to support Vivalan<sup>®</sup>. Sadly, wasn't a great success. In fact, ICI were offered paroxetine at the time, and because it had a high incidence of nausea and emesis (25%), the marketing people and management at the time said, 'We don't want it.' And, that's another story, because that's what I successfully did for 10 years as a Director of Neuroscience at Beecham/SmithKline Beecham to help develop paroxetine (Seroxat<sup>®</sup>/Paxil<sup>®</sup>) for depression and anxiety.

**TT:** We can come to that.

**TB:** Des Fitzgerald still comes up to me today to say, 'Why did we not pick that compound up?' But we had a lot of internal changes in those days, Dave had moved off, Barry came in and then Barry disappeared to head up cardiovascular research. Then, Dr Mike Rance came in, Mike was very much an opioid man. He'd joined from Reckitt and Coleman, with a background working on buprenorphine and worked with Professor Hans Kosterlitz in the opioid field. So I ended up developing tests then for opioid analgesic efficacy and side effects, but 5-HT was still there in the background. I was given responsibility, when Barry moved over, for the two development compounds, ICI 169369 and ICI 170809. Actually, I brought this for you because I'm giving a lecture on drug development at St. George's on Thursday.



It shows all the compounds I've had some dealing with in drug development. There's eight compounds I've taken into or been part of their clinical development.

**TT:** That's a considerable record.

TB: Yes, yes.

**TT:** Who are you lecturing to at St. George's?

TB: I'm talking to the MSc students on 'Drug Development Horizon', as part of their course. It's basically drug development and the future of.

**TT:** That's very helpful, Tom. Let's go back, so you're switching onto opioids.

TB: So I'm switching now to opioid research and Mike Rance wanted me to move more towards opioid analgesic research. Thus, I was stuck in the middle of trying to continue the development of 5-HT compounds, yet build an opioid background. This is the thing about what you see in industry, or what it used to be like, or perhaps it's still like to day, is that people in academia can stay with a project forever as long as the grants come along and they can build that academic research profile, which is great because that's what you need to make breakthroughs - time... But in industry you're constantly, and more so now, chopping and changing. However, I like working with Mike, he came along and he introduced me to  $\kappa$ -opioid receptors. And, I became very interested in  $\kappa$ -opioid receptors, I'll come to this again because of the bizarre behaviours and diuresis that you saw with this class of compounds in animals. It was like a 'trance-like' behaviour, if you could put a name to it. So, I was trying to link this opioid receptor subtypes ( $\mu$ ,  $\kappa$ ,  $\delta$  and  $\sigma$  receptors). We developed a  $\delta$ -opioid antagonist at the time, which didn't seem to do very much. It was sent all around the world to look for efficacy in different test systems, essentially with little luck at the time. But, the  $\kappa$  receptor really peaked my scientific interest, and one of the actions was the diuresis associated with  $\kappa$  stimulation. I developed a system/model to test these compounds, whether they were acting centrally or whether they were acting peripherally. So I got to know this guy in Manchester, Professor Richard Balment in the Physiology Department. Sadly, I've lost touch with Richard over the years, but Richard was very helpful and another very important person in my life.

**TT:** I hadn't picked up Richard's name in your CV. He and I were in Sheffield at the same time.

TB: Yes, it was Richard at Manchester that I worked on  $\kappa$ -opioid receptors and diuresis. So what I did was very similar to the types of *in vivo* models you were studying, Tilli. The work you did with the 6-hydroxydopamine Parkinsonian rat model. So I worked with Richard on this project, and to be honest, I think it was my idea from reading the literature, which suggested that the adrenal medulla may be important in diuretic-like effects of  $\kappa$ -agonists. With Richard's help, I de-medullated rats and we tested then for their diuretic response to  $\kappa$ -agonists. And, surprise, surprise, you lost the  $\kappa$ -induced diuresis in saline-loaded animals, but produced antinatriuresis. So here was a way of basically looking at peripheral  $\kappa$ -opioid receptors. Which, is interesting because these phenotypic models you're looking at a physiological effect; going back to my background in physiological techniques and using the physiology/pharmacology to work out what these receptors were doing. So I developed this *in vivo* model at ICI.

**TT:** And this was in rats?

TB: Yes, this was in rats. At that time, I asked ICI if I could I do a PhD based on this model, and thankfully Mike Rance supported me and the department (James Conway). So I began my PhD thesis in 1986 and finished it in 1999. I did my PhD, again taking some time off in Manchester, working weekends, taking holidays, all to get my PhD.

**TT:** And who did you do your PhD with?

TB: Richard Balment.



**TT: I had no idea. He was the year above me and his wife was in my year, so I knew Richard and Janet quite well at one stage. I'd occasionally bump into him at Phys Soc meetings.**

TB: So that connection, was important for a number of reasons. It allowed me to follow a piece of research that I found fascinating, but it took me somewhat away from my 5-HT development work. At that time, ICI bought a company called 'Stuart Pharmaceuticals' in the US, so this was in 1975/76. Stuart Pharmaceuticals were heavily into CNS research, so who is this guy from Liverpool on the other side of the ocean, looking after these two CNS development compounds, about to go into man? Unfortunately, looking back, the clinical studies (migraine, depression and schizophrenia) we took 169 and 170, weren't really powered enough to show efficacy. Whether this was because of the issues we've found out over the years with DSM [Diagnostic and Statistical Manual of Mental Disorders] criteria or poor clinical design etc. So, sadly, those two compounds lost the way. It's interesting that when things are going very well there's lots of support, but when there's a hint of a toxicological issue, then people start to put their money, place their bets, on other compounds with less risk, which is fine. But, what happens you find, and I've experienced this a number of times, is that you get a delay in your development programme, while those tests are repeated again. And, sometimes those tests are repeated again and they don't find anything, but by then you've lost 6 months of development time, and the money has been allocated for other development compounds. And, all of a sudden there are naysayers, 'Oh, you'll never get anything out of serotonin research' at management meetings when you're presenting. That's pharma politics.

**TT: It's the same in other fields as well.**

TB: Yes, yes. So that's politics.

**TT: Can I just ask you about taking these drugs into man? What was your involvement in that?**

TB: Actually taking them from being a guinea pig and taking radio-labelled ICI 169369 and designing some of the clinical tests with the clinicians. Again, like chemists, I worked very closely with the medics Drs Steve Howard and Roger Yeats. I used to spend my time going into the clinical unit and developing tests like pupillary diameter measurements, we were looking at the effects of drugs we were working on. We published a paper on the model with Dr David Milson. So that was one test. Again, I'd researched the literature, brought it to the clinicians attention; 'Here's a physiological response, can we look at this in the clinic to see if there are any effects?' So we published a paper on it. What was the other? EEG [electroencephalography]? This was the time that EEG was starting to become more quantitative rather than qualitative, and we set up a small unit to look at EEG changes because with a lot of the antidepressants what you were seeing with some of them, like viloxazine, an arousal-like effect and you actually saw this in the clinic as well. So here were two translational clinical pharmacology models, we using in the 70s, which became part of the clinical trials and I have used those tests in subsequent studies as well. I was always getting involved with the clinical people and safety people. It was known that I used to go into the safety and medicines department to see why my compound wasn't showing any plasma levels. And, basically being told that, 'Oh, it's not getting into the system.' So I would go along and you watch the technician dose it and you see that the rat spits it out straight away because of the bad taste.

**TT: So do you get involved in formulations as well?**

TB: Yes, I would always get involved in formulations and sometimes upsetting senior managers in safety of medicines department, because you actually went in as the drug champion and showed that the floor of the rats' cage was covered with compound. So that is one of many examples, and there are many others. To get back to the ICI compounds, unfortunately they lost their way and so Barry Cox had moved off into the cardiovascular side of things. Dr David U. Pritchard who came to ICI at that time, and I'd been offered a couple of jobs in the States, and I was also interviewed for a job at Beecham. So this is '88/'89. And the ICI compounds were still hanging in there, just, but it looked like the Americans wanted to do it their way. Barry Cox and myself actually went over to the States and showed them some of our data with regard to them

eventually developing the mixed 5-HT<sub>2A</sub>/D<sub>2</sub> compound, quetiapine (Seroquel®), which made a fortune for AstraZeneca.

**TT:** When you say you showed ‘them’, you went to the States to show ‘them’, who are ‘they’?

TB: Their senior research people, because they had a number of primate models and I was trying to show them that serotonin was important in modulating dopamine release and *vice versa*. I don’t know why I wasn’t asked to go over there and become part of their CNS team, but it didn’t happen. I was approached by Beecham and because CNS was closing down, I joined Beecham Pharmaceuticals.

**TT:** CNS at ICI?

TB: Yes, CNS at Alderley Park was closing down, and I really wanted to pursue the depression/anxiety area. By then I’d really got to grips with understanding the depression/anxiety area, and this takes me right back to my mother, because my mother’s house was blitzed in the May blitz in 1941 in Liverpool; she was nearly killed next to her mother, her mother was killed. But, I realised that panic disorder and post-traumatic stress disorder [PTSD] were very much part of my mother’s life. And, there used to be a programme called *The World at War* on BBC that used to come on.

**TT:** It’s still on.

TB: It’s still on? I remember, when the sirens start at the programme, it used to freak my mother out. And I couldn’t understand then... My father used to turn the television off straight away, or if he knew the programme was coming on he’d turn the TV off, but I always wanted to watch the programme. So later on in my career I started to understand a bit more about mental health in later life. Panic disorders and PTSD, and other problems associated with mental health. So that drove me even more to be looking for new, novel antidepressants, anxiolytic agents. So Beecham approached me, a chap called Dr Tony Ainsworth, a chemist, he was the Head of Research at Beecham in Harlow, and Dr John Flack was the Head of R&D, they persuaded me to come down and join Beecham as a Director of the Anxiolytic Programme at Harlow. I was just finishing my PhD then, so this was 1989. And, at ICI, Dr Dudley Earl who was Head of the Department then, and Dr Mike Turnbull, basically asked me to stay. They offered me a section head job to look at potassium channel openers, which Beecham were heavily involved in. I was tempted to stay because the site at Alderley Park was absolutely beautiful, and a great place to work. It had all kinds of wonderful memories for me there.

But I accepted the job and I moved down south, much to the disgust of my daughters. The fact that it was a bigger, better job, was something they did not understand as teenage girls. We were moving down south, we were told that people in the south of England weren’t very friendly. House prices were ridiculous, you couldn’t get anywhere near the house we left for the same price.

The kids couldn’t understand it. They wouldn’t join me. They were like 12 and 13/14, so they’re at a very difficult age for dads. And we moved down, but the children stayed with their grandparents for 6 months while we could find schools. So we were travelling backwards and forwards, up to Cheshire, Congleton. I enjoyed Beecham very much, because of the responsibility and freedom I was given. This was the first time I was heading up a team of 40 people and I had my own chemistry team, I had my own formulation DMPK (drug metabolism and pharmacokinetics) people, I had clinicians, and we were a really good and productive team. In fact we were so good, we were invited across to Merck at Terlings Park. My Head Chemist (Merv Thompson) and myself, were invited across to Merck by Drs Les Iversen and Geoff Woodruff to tell them why we had better compounds than them. Okay? This was in the potassium channel area and GABA [ $\gamma$ -aminobutyric acid], which again is an area I’m very proud of. As for the potassium channel area, we’re getting back to ICI now. When I came down to Harlow, I got Drs Merv Thompson and Neil Upton into my office and I said, ‘I want a compound that will be an anticonvulsant based on the potassium channel.’ The Head of Genetics at Beecham’s at the time, wouldn’t touch potassium ion channels, because there were

potentially so many. It was an area (molecular biology) that was just exploding. By the way, there are 14 5-HT receptor subtypes that were identified during this period.

So Neil and Merv went on their way and basically we developed compounds, again based on anticonvulsant models (translational models), SB 204269 (Carabersat®) and there was another compound SB220453 (Tonabersat®), which eventually went into man. And, again if more time would have been spent with these compounds internally, I think we would have got somewhere. But management changes happened and various other things. As we didn't have a mechanism of action, right? We didn't know how they were working, so it was, like the 5-HT<sub>1</sub>-like compounds, we had potassium channel-like compounds! New management came into SB [SmithKline Beecham] and Dr Peter Goodfellow and others, were saying that we couldn't move forward with these compounds because we didn't have a molecular mechanism of action?

**TT: And it was still Beecham then?**

TB: No, no. Sorry, I jumped time a bit. It was SB, and because the potassium channel area was a very exciting, I could see things moving along quickly in development - as the compound was very safe. They were easily formulated, and there were no apparent safety problems with them. But it happened again and not for the want of trying on my part or Neil (who championed the compounds in development) and Merv Thompson the chemist. The compounds seemed to lose their way a bit because of management changes and the need to know what the molecular mechanism was? Peter put a lot of effort in trying to understand that. However, several years later data showed this class of compounds had gap-junction inhibitory properties. But, well before then, the Therapeutic Area Team [TAT] had dismissed further development of the compounds. Later, when the head of the CNS TAT left SmithKline Beecham, he took the compounds with him to form his own company.

**TT: Was that allowable? How was that negotiated?**

TB: Well, who knows? I've seen that quite a lot development people have walked away with compounds and set up their own company. Where are the compounds now? Not sure, may be with some biotech company in the States, looking to leverage them for financial backing? So sadly, that is one piece of my drug development life which I would have liked to have seen develop into a novel antiepileptic - something with a better efficacy than some of the standard anticonvulsant agents, or perhaps effective in a subset of refractory patients. So that was one, if you like to call it a failure, I don't know? The team and I won the SB 'Simply The Best' award in 1993 for the novel anticonvulsant programme. Sadly, the GABA<sub>A</sub> project that Merck was very interested in, was also closed during the SB days, due lack of support; anxiety was too difficult an area for Pharma companies to develop compounds in.

**TT: This was a different team? You were running a number of different teams?**

TB: Yes, I was running the GABA<sub>A</sub> team anxiolytic programme, which we had very good subunit selective compounds. I was also responsible for the CNS 5-HT<sub>3</sub> receptor antagonist programme and the lead compound BRL 46470, which came from Dr Gareth Sanger labs at Beecham.

**TT: This is a receptor antagonist?**

TB: Yes, 5-HT<sub>3</sub>. This was the time Professors Brenda Costall and Bob Naylor had been working with Glaxo on the central effects of this class of compound. But Gareth (Sanger) had found a 5-HT<sub>3</sub> compound that didn't appear to cause constipation. I said, 'I'll have that compound.' We repeated a lot of the tests that Brenda had published on, and in fact we repeated a number of her tests which other people couldn't. But one of the big issues with the 5-HT<sub>3</sub> area was the doses we were using. The doses were very small (micrograms). And, perhaps even sub-microgram level. The management and clinicians couldn't get their head around that. In fact, the SB couldn't get their head around it either. It was difficult to understand but when you think of psychotropic agents, like LSD [lysergic acid diethylamide], you're dealing in micrograms and you're seeing very profound effects in man. But getting this across to an organisation that produces >200 mg pills

is very difficult. So although a development team was set up, we took the compound into the clinic, and looked at a couple of CNS indications, but unfortunately the compound failed to show clinical efficacy in underpowered studies. At one point, I had shown this *TIPS* [*Trends in Pharmaceutical Sciences*] cartoon to a TAT presentation which showed a guy in a white coat with a white board with all of the possible indications for this particular compound on; from anxiety, depression, sexual dysfunction, you name it, was on there. And, the cartoon manager was sitting looking at this guy and saying, 'What else are you going to tell me it's going to cure?' So that is the situation you get in. So you're in a development team and basically people are looking at this compound and saying, 'Well, really we could do with a new anti-schizophrenic compound and this seems to be effecting dopamine' or whatever, although there were doubts in the validity of many of the CNS models you were presenting. So that compound unfortunately lost its way, perhaps because of the *in vivo* models, dosing regimes and difficulties with clinical end points and diagnostic criteria. Who knows? I don't know and I don't think Glaxo did any better with their compounds.

**TT:** So that's three teams you've mentioned.

TB: Yes. And there were others. One of my favourites, 5-HT<sub>2C</sub>. The 5-HT<sub>2C</sub> receptor and the 5-HT<sub>2B</sub> receptor goes back to my ICI days, before the subtypes were identified. Observations then in *in vitro* models that I was working on, was a response of the ICI 5-HT antagonists on rat stomach fundus receptor - Sir John Vane's rat stomach fundus preparation. I was seeing a difference between non-competitive and competitive 5-HT antagonists in that rat fundus preparation at ICI. I was saying, 'It's not 5-HT<sub>2A</sub>, it's a 5-HT<sub>2</sub>-like receptor. There must be another receptor there.' So when I went to Beecham, a young guy and his wife, Gordon Baxter and Carol Routledge, were working in Syntex in California, and they approached me for a job. So I brought Gordon in and Carol to Beechams. Carol went off to work with Dr Brian Jones and Gordon was working with me. I put him in the corner of a lab with Olive Murphy and I said, 'There's the water baths, get some rat fundus and I want you to find the 5-HT receptor.' And Gordon eventually found what was called the 5-HT<sub>2B</sub> receptor. However, Dr Marlene Cohen in the States working at Lilly was also working along similar lines. But, we got the first selective antagonist. We synthesized a selective antagonist for the 5-HT<sub>2B</sub> receptor and then a French scientist, Luc Maroteaux, showed that this particular 5-HT<sub>2B</sub> was found in the heart and may be an issue with regard to cardio valve atrophy. Although, this was shown to be due to stimulation/5-HT<sub>2B</sub> receptor agonist effects, SB decided not to pursue this compound with all the controversy with weight loss compound at the time; fenfluramine. Gordon left the company, not long after.

However, the compound was an important pharmacological tool, and really helped us in many ways to tease out which of the 5-HT receptors were important. This was the time just before and after the Beecham/SB merger 1989-91.

**TT:** The merger with SmithKline?

TB: Yes, yes. At that time the team had just identified a selective compound for the 5-HT<sub>2C</sub> receptor I was very interested in, because by this time nearly 14 serotonin receptors had been identified and the 5-HT<sub>2</sub> family consisted of 5-HT<sub>2A</sub>, 5-HT<sub>2B</sub>, 5-HT<sub>2C</sub>. The 5-HT<sub>2C</sub> was very interesting because of its distribution in the brain, in areas of the brain associated with anxiety, depression etc. Again, I worked very closely with my chemistry team, and we were looking for selective compounds, and identified a number of selective compounds for this receptor subtype. In fact, we provided Aldrich/Tocris and many other companies with a lot of very selective compounds for teasing out the different 5-HT receptors. I've listed them there [see diagram above]: SB 243213 was a compound for anxiety/depression. Unfortunately, in a Phase 1 study, a cardiovascular effect was observed. I still have my doubts as to whether it was drug-related or a normal physiological effect observed sometimes in volunteers/people (vasovagal syncope) in clinical trials. And, postural hypertension, that's when you get up too quickly or if you've had blood taken, and there's a lot of blood being taken over the course of your time in a clinical unit. Unfortunately, this was something that wasn't progressed, because it came at a time when money was short and projects were being financed on the basis of 'de-risking' criteria for each therapeutic opportunity. And, the time when the cost of actually developing a novel antidepressant was starting to become prohibitive. The project was closed.

As SB already had the antidepressant paroxetine, and for 10 years, between '89 and '99, when I left, I was the front person for paroxetine at Beecham and SmithKline Beecham. So not only were we doing bench/preclinical work with excellent scientists like Dr Guy Kennett in my group and others, it was during this period I actually presented the compound to visiting clinicians, neurologists, scientific advisory board members from the UK, Europe, and America. I then fed the clinical observations from them back to my team, as we were trying to understand why with a lot of antidepressants had to be titrated to the patient, and on the spectrum of anxiety and depression you had disorders like panic attacks. Why were patients treated with 60 mg of paroxetine for panic attacks, and only 10 or 20 for depression? Is there some pathophysiology/neuroanatomical difference in these disorders, is the circuitry somewhat different between these brain areas, what receptors were the side-effects due to? So we developed one protocol where we were chronic-dosing for 2 weeks with paroxetine in a rat model that basically gave us an anxiolytic-like effect, and we repeated that in non-human primates as well. I think that data helped the clinicians rationalise this difference and downstream Paxil® (Seroxat®) into the anxiety disorders.

**TT:** Can I just ask what was the status of Seroxat at that stage? It wasn't yet on the market and this was all development work?

TB: No, it was just breaking onto the market, but with any drug development process, what you're looking for is to extend its profile, the market franchise, whatever you like to call it. So depression/anxiety and whatever you were looking for something novel. In my book, paroxetine is still a very good antidepressant. There's been a lot of criticism because, I think, there was something like 17 studies, and only two or three actually were accepted by the FDA for registration. And, during this time, there were major concerns for antidepressants increasing suicidality thoughts, which is now apparently the concern with all CNS agents and is at the forefront of regulatory approval for any CNS drug. Whether it's an antidepressant, anticonvulsant, or any other CNS drugs. As the science and clinical experience moved on, we know now that the developing brain, particularly of depressed adolescents, is vulnerable to suicidal thoughts. And, it's this issue that sadly turned many pharmaceutical companies away from developing novel antidepressants for mental disorder. A disorder that is still so insidious and prevalent today. Ask any GP [General Practitioner] or primary care physician.

**TT:** There's a lot in the press about that, isn't there?

TB: Always. And, to me, that is one of the sad aspects of drug development. Sometimes a compound is tainted when we don't fully understand how compound works. How the drugs are prescribed, given and taken; there are always compliance issues. But what we are trying to understand more and more about our bodies and about the personalised medicine, we're all different. So we are now looking at precision medicine and the genetics of it, and how one patient can take, say, one antidepressant, and another patient can't, because of differences, say, in their liver enzymes or particular 5-HT receptor subtypes or transporters that are not as sensitive to that particular drug. With many of the older drug therapy, it's like a blanket effect, a biochemical straightjacket that older drugs have on many receptor subtypes, particularly in mental disorders. This has sadly been so for many years now. It's only now with advances, say, in cancer chemotherapy. We're starting to see how precision medicine is coming in more and more to medicine. So, yes, there are issues with all antidepressants and drugs in general. There are issues with all antipsychotics, there are issues with all anticonvulsants, but what you're trying to do is give/titrate the drug to the patient needs, so that a particular drug will be more effective, and hopefully relieve the symptoms or eventually cure the disease.

On the plus side, when I left the UK in 1999 to go to the States, my wife and I were looking around an apartment in Hoboken New Jersey to live in. And we wanted three bedrooms so our daughters could come over and stay. The lady/agent who was showing us around wanted us to fill out the contract, and there I had to put my occupation down. You're always very wary of what you put down and what you've worked on, particularly these days. I put down 'neuroscientist' or something like that and she said, 'Do you work on drugs?' I said, 'Yes, I have done.' And she said, 'I can't thank you people enough.' She said, 'My husband is a failed actor on Broadway and he's been on a compound called Paxil. Do you know anything about this compound?' So I said, 'Oh yes, a little, a little.' She said, 'It's given me my husband back.' So she then said,

'I want you to sign another contract, but first, I want you to come down and have a look at a two bedroom apartment.' I said, 'Two bedroom, why?' She said, 'You'll walk in the door and you'll fall in love with it.'

I said, 'Okay.' So my wife and I went down, and we walked in the apartment, and there was this view of the Manhattan skyline with the Empire State right in front of us and the Hudson River; it had everything. And we said, 'Yes, we'll sign the other contract.' So we signed it and that's one story out of a number of stories where people have told me that they have had therapeutic benefit from Paxil. So all drugs have issues, but there are benefits... for example, I can't particularly take aspirin because it upsets my stomach; I can't take statins because I get these muscular problems and pain. So each and every one of us act differently to drugs, and we should question doctors who prescribe them. Sadly, some people will just take tablets and not understand the problems they may cause. We're more fortunate today that we can Google everything and find out more information about drugs we are prescribed, which is great. It helps our understanding as what is good for us, what is not so good for us.

**TT: It was quite a leap, wasn't it, moving to the States? Or did it seem an obvious move in 1999? Had you come to some sort of endpoint with SmithKline Beecham?**

TB: Well as I said earlier, the Beecham/SB days were great days 1989-1999. We had some great management, Drs Tony Ainsworth, Brian Morgan and John Flack who brought me from ICI to Beecham. Then, the merger with Glaxo was on the cards in 1999. As with the merger with Smith, Kline & French, if you wanted to become a major player, you really had to have great marketing people. That's what Smith, Kline & French brought to the table. They gave us that big foothold in the States. And, I think five out of the Beecham drugs became billion dollar plus drugs after the merger. When I left SmithKline Beecham in '99, I left one of the drugs that was a \$4.9 billion product, Seroxat®/Paxil®. Today the life expectancy of a drug peak sales (four years) is less, because of generic competition and 'me-too' like compounds, such that you hit the top of the profit curve earlier. So no matter how much money you're throwing at the marketing, your market share is eroded quickly; this eventually happened to the SB antidepressant. Your returns are eroded because of competitors. And the competitor that came onto the scene in those days was Forest Pharmaceuticals and Lundbeck, with their citalopram, which appeared to be safer because it was reported to have less P450 liver enzyme interactions, and Forest had big sales force in the US.

All drugs have a few chinks in the armour, which basically competitors would go after, and Forest were doing a remarkable job for Lundbeck who entered the market with citalopram. So my role started to disappear, we lost the momentum. Also, the 1990s was the time that the SB genomics revolution started, so everything was molecular and we were looking for a molecular mechanism all the time. So the 90s were very productive for me with regard to Paxil®/Seroxat®, potassium-like compounds, 5-HT<sub>2C</sub>, 5-HT<sub>2B</sub>, although GABA<sub>A</sub> lost its way. Then Drs Frank Walsh and Peter Goodfellow joined SB, who basically wanted to move away from 5-HT, and move more into genomic research with their team. That's fine, but it really was for me as by then I was what, 48/49, and SB were retiring a number of my peers in their 50s. So, I'd always wanted to go to the US and into the biotech world, because I always felt that's what I do. I think there's a famous quote that a pharmacologist (Sir John Gaddum) is a 'Jack of all trades,' so I'd been involved in all kinds of bioscience skills and techniques: drug discovery, clinical development, lab/department management, regulatory affairs, formulation; so many aspects of drug discovery and development. And all of those things came together to say, 'Okay, Tom, things may not be going so well for you at SmithKline Beecham with management changes etc.' and I'd been offered a few jobs in the States, prior to this, with one or two other companies. So I had this calling 'Let's go to the States and join the biotech world.'

Thankfully, my wife backed me and my daughters were in relationships then, and it was just as quick to fly across the Atlantic as to go around the M25. So I accepted a job with Synaptic Pharmaceuticals in 1999. Dr Terri Branchek who had been working in the 5-HT area for a long time, who I knew very well, was Head of Research. The company were one of the leading companies in de-orphanising GPCR [G-protein-coupled receptors] receptors, they were very molecular based and I wanted to get more into that myself. I was given the job of Head of R&D. So that was perfect, as I thought then.

**TT: You must have been very familiar with American companies, you'd worked for British companies with American partners or headquarters. Did you find a great culture shock moving to America?**

TB: No, not a culture shock, not really. Some people in the north of England would talk of the cultural shock about people in the south of England; this is just the same as what people say about the America. I think it all depends on you as a person, and I just felt the States were right for me and my family. I was approaching 50 and this was going to be a new chapter in my life. I wanted to be into the biotech world because I don't like to say this word, but the bureaucracy of the big organisations with matrix management was becoming overwhelming and unproductive for me, trying to get decisions made across different departmental silos. It was very political. I'm not saying it isn't political in biotech, but I/you could get things done faster, smarter and reach critical scientific/business decision points quicker. I would go into lab and say, 'Look, why don't you try this? Or can we do that? Or that's a great experiment, well done. That's really set us off on the right track.' So you can have all these corridor/lab conversations and get things moving a lot quicker rather than trying to spend all your day or your secretary time booking or arranging meetings in a meeting room which you have to book months in advance. I went back to my old SB/GSK Harlow building not long ago, it was a brand new (SC1) building when I left. Then you couldn't get a meeting room unless you booked years in advance! I went in there about five years ago and it was like a ghost town, it was dreadful to see all these meeting rooms empty. And in my day it was so difficult to book one when you wanted one.

**TT: It's not unique to industry.**

TB: No, I know. But people like to spend their time in meetings. 'Oh, my calendar's full of meetings. Yes, I'm sorry, I'm such a busy person.' But, anyway.

**TT: You go to Synaptic as Head of R&D? Did you have any particular remit? Were you expected to deliver in a particular area, on a particular project? Because you took quite a portfolio of experience with you.**

TB: Yes, well VP [Vice President], Head of Pharmacology. Synaptic were doing all of the 5-HT receptor subtype screening for Eli Lilly, and they had an  $\alpha$ -adrenoceptor programme with Merck, and some other very interesting programmes. Again, some in the depression/anxiety area. So I liked the idea of (a) going in and learning the biotech way, and (b) living in the US.

In fact the BPS [British Pharmacological Society], we haven't mentioned the BPS yet, but my last meeting was down at the Metropole Hotel in Brighton when I left in '99, and Peter Goodfellow was giving the clinical prize to Professor Rob Kerwin who sadly later passed away. Peter was to present the SmithKline Beecham Clinical Prize, Peter came to present the Prize, and at the reception before the dinner he pinned me against the wall at the drinks reception and said, 'Why are you leaving SmithKline Beecham?' I said, 'Oh, I want to, basically, move to the US as I never postdoced there like so many of my contemporaries. Although over the years I've spent a lot of time there. I just wanted to look and learn the biotech side,' which was true. Yes, there were management issues and various other things, and my particular field of science wasn't being supported, but that's fine. He said, 'We don't want you to leave.' I said, 'Well, I'm sorry, I've signed on the dotted line.' Later, Peter got up to present the Prize and it took him 25 minutes of diatribe basically lambasting pharmacologists for not embracing molecular biology. If he would have looked at the abstract book there was 75% of the abstracts that had some molecular biology in them. Jimmy Black was on the top table next to me, and Dr John Fozard, who was sitting next to my wife, Jacqui, and you could see all people twitching during his speech. I eventually cut him short and he presented the Prize to Rob, then went off stage. And, as I was coming off the platform - in those days we had platforms at the official dinner - a young PhD-student, a girl, came up to me, and said, 'Dr Blackburn, was Dr Goodfellow trying to impress us with not embracing molecular biology? Because, he failed miserably.' So I said, 'Well, thank you very much.' So that was a young PhD-student's response.

**TT: You did tell a version of that story in our 5-HT Witness Seminar volume.**

TB: Okay, but did I tell you the Andy Ramage one?

**TT: No.**

TB: We were coming out of the lift that morning and just about to go off, and Andy came in, I don't know where he'd been, but he came in and he looked at me coming out of the lift, and the lift was full of people and he said, 'Tom, after that talk yesterday (of so and so),' he said, 'I know now why you're f... leaving!' [laughter]. There were all kinds of people in the lift. 'Thanks, Andy.' Anyway, the sad part to that was leaving the BPS behind in the middle of my tenure as their first President.

**TT: You were President of the BPS?**

TB: Yes, I was one year into my presidency, but as I mentioned earlier people of my age within SmithKline Beecham, were being given early retirement at 50. And, there were some very good scientists and very good people. I could see the writing on the wall for me, so I basically made my way to the States, because of things happening at Harlow, and my science not being supported. And so that was that.

**TT: So you reinvented yourself or, you didn't really start again, you were acquiring another attribute moving to Synaptic, biotech, fresh challenges; you seem to thrive on challenges?**

TB: Yes, yes. And in this company, basically, we had a lady called Dr Kathleen Mullinix who had spun out of Columbia University. She was Head of Intellectual Property and Kathy was a tough woman, in the R A Gregory mould, but very good. And, there was Terri and the Chief Financial Officer Bob Spence and Richard Weinshank, who were all very supportive. But what happened was I wasn't five minutes into the company when the collaboration with Merck fell apart, and the collaboration with Warner-Lambert fell apart, and the Eli Lilly project was coming to an end. So within months literally of me being there, as Head of Pharmacology Research, I was basically going back to basics. So I looked at their portfolio, they had already had some of the compounds that had come back from big pharma of no interest to them, that had been through their bog standard screens, with no or little hint of activity. So I said to the senior management of Synaptic, 'Can I take a look at some of these compounds and take them outside and test them in some tests which I think might show something?' And, I got their support and one of the compounds was SNAP 37889, a galanin 3 receptor (R<sub>3</sub>) antagonist. I tested the compound in an electrophysiological study I previous used at SB. I brought back the data into the company and showed them and said, 'Look, this is a very similar profile to what I was seeing in the past with SSRIs, but it's working through the galanin R<sub>3</sub> receptor.' I then took the compound into more studies internally and externally to build a profile up, and then see if it was a potential development candidate. We already got some data back from the big pharma collaboration with regard to some safety data. I then got the support from the board to move the compound forward as the company were seeking a further round of finance, and a proposed development candidate would add to its value.

So then I became VP & Head of Drug Development and Officer of the company at Synaptic. By then I was training some of the staff in drug development skills. There was a young girl who had a bad animal allergy who was about to lose her job, so I asked if she could help me handle all the filing and the regulatory work building up to an IND (investigational new drug) filing and document management.

To cut a long story short, she now has a senior regulatory position in pharma. It was a bit like at Beecham: I had my chemists, my DMPK people and I'm training chemists up into producing API (active pharmaceutical ingredient) and clinical trial material, and work as formulation people. So I built a drug development group up within 18 months of getting that compound back from big pharma, and was IND ready for Phase 1 testing in 2001.

**TT: Quite an achievement.**



**TB:** I put all of the building blocks and just as we were going to start clinical trial in Phase 2 with Duke University, the Danish pharmaceutical company, Lundbeck, bought us. Warburg Pincus came into fund the company in 2001, and then sold the company to Lundbeck in November 2002. Lundbeck wanted Synaptic's expertise in molecular biology skills, and they wanted the novel compounds we had at the time. I think one of the compounds I haven't mentioned on that list, I should put it on that list, was a melanocortin 1 receptor antagonist, MCH-1, which we published in *Nature Medicine*. So there were two development projects. There was the MCH-1, and I was on the patents for anxiety and depression for both the galanin R<sub>3</sub> and the MCH-1. So, unfortunately, what happened with these compounds, was they were up against the Lundbeck's internal compounds, and lost their way for various internal reasons. Lundbeck had their own compounds which their people developed, and there was a lot of tradition and internal pressures in the company. So Synaptic's compounds unfortunately disappeared within the Lundbeck portfolio.

**TT:** You were there for just a year or less than a year?

**TB:** Yes, but while I was with them, they gave me this beautiful office in New York City overlooking Madison Avenue on the 34<sup>th</sup> floor, and in my job, Director of Medical Affairs, was to build relationships for Lundbeck in the US with the likes of Columbia, NYU [New York University], etc., which I did. I tried to get the company to be part of a neuroscience hub on the east side of Manhattan. Alexandria (a Life Science Building Developer) were building a new bioscience park. And, I was hoping Lundbeck would be the anchor company in that park. I did a lot of the ground work for that project with the NYC universities, but Lundbeck had other ideas.

**TT:** This was mainly with Columbia, was it?

**TB:** Columbia, New York University and perhaps one or two others we talked to, Stony Brook, and Cold Spring Harbour.

**TT:** What happened then?

**TB:** I asked Lundbeck, 'Could I spin out of the company with the galanin R<sub>3</sub> receptor compound? Could I have a license to develop the galanin compound?' And Lundbeck agreed, I'm still one of the few people, if not the only person, who they actually allowed to take a compound out of the company. But the terms that they offered me were sadly prohibitive at the time. I went around the various investment banks and VC [venture capital] people in New York, but could not acquire the finance. So I ended up not taking up Lundbeck's offer. At that time, Dr John Tallman approached me. He headed up a company called 'Helicon Therapeutics' in Farmingdale, on Long Island, and he wanted an R&D development person because he had some interesting compounds. John had run a company in Connecticut called 'Neurogen' and it had done reasonably well, but was bought out of retirement by members of the Board of Directors of Helicon. John knew of my work in the 5-HT and GABA<sub>A</sub> area and Synaptic. He asked me if I would join Helicon and basically set up a development group with them. So, I said, 'Yes, it sounds exciting, back to biotech.' And so I joined Helicon, and was there for about three years? Yes, about three years, which was an exciting time because again I was VP, Head of R&D. During this time (2003), I was awarded a DSc for my work and publications on the 5-HT receptor subtypes. Professor Alan Crossman at Manchester University helped me achieve this important academic milestone in my scientific career. So, thank you Alan, Manchester University and the many co-workers and friends I published with over many years.

Now, back to Helicon. The guy who founded the company, Dr Tim Tully, is a *Drosophila* genetics man, and he'd been backed by a number of different people and had spun out of the university, of Cold Spring Harbor, to form his company. Helicon had acquired a compound (IPL 455,903) which became HT-0712, a phosphodiesterase 4 (PDE4) inhibitor, which Tim had shown was a cognitive enhancer (nootropic) in a *Drosophila* model, and in some rodent tests. So again, this was of interest to me and I set up a whole series of tests to support these observations. I got the compound moving forward for IND submission and ready to go into Phase 1, and then Phase II clinical studies. I was also interested in some other projects, and put into place a glycine transporter inhibitor project. I'd also said to John, 'John, I know of a compound which

I think you would be interested in' and that was the galanin R<sub>3</sub> compound. So John completed the due diligence on it with Lundbeck, and in-licensed the galanin R<sub>3</sub> antagonist for Helicon (HT-2157).

**TT: So it was rescued?**

TB: Yes, so I was using another company's resources and money to move this compound forward again. So we were developing that compound as well for clinical studies. And everything seemed to be going hunky-dory. John and I were excited about the potential of the compound to treat depression. However, there was a problem with the formulation and I'd been out to Singapore to look at a nanotechnology formulation those early days, and John and I travelled to South Carolina to look at this formulation company for the galanin compound. Because it had an aniline moiety this could be a potential safety problem, as it could cause methaemoglobin if metabolised in the acidic stomach at high doses, and chemists don't like aniline compounds. However, if you could get it past the stomach in novel formulation, that takes it past the acidic stomach, you wouldn't see any methaemoglobin, okay? So that was the formulation trick, we hoped would work. We went down to South Carolina and were basically impressed with the formulation technology at a company there. John was flying back to Long Island, into McArthur airport and we had to transfer in Atlanta, as I was flying on to Newark. The following day we had two teleconferences with AstraZeneca and Glaxo. I was waiting for John to arrive. John never turned up for either one of the calls. To cut a long story short, I got his secretary to phone around and we got the police eventually to go to his house to sadly find John dead.

**TT: Oh my God.**

TB: Hm. So that was quite a shock for me, the company, and, of course, his wife. The last time I saw him in Atlanta airport, he was so pleased with the trip to South Carolina and could see a good way forward for the compound. That was a very sad day and very intense period of time in my life.

**TT: How absolutely tragic.**

TB: Lots changed during this period in my life and the company as you can imagine. Not long after the company were forced to move out of Long Island and find other premises, as we'd lost our animal facilities at Cold Spring Harbor. And, the Farmingdale officials wouldn't allow us to build a vivarium, so the board asked me to find another place. So I went all around the NY tri-state area looking at other facilities, but the Board wanted to move to California, to San Diego. So I was going backwards and forwards to San Diego looking at facilities and eventually found one, a beautiful 80,000+ square feet, facility. I did all of the groundwork for moving the staff and everybody out there, took my wife and my family out there to show them. But, to cut a long story short, my wife and I didn't go. Which caused a few ripples and surprised a few people. It just was not for me for various reasons.

**TT: It must have been extremely traumatic.**

TB: It was, yes, it was in many ways. I think, I left the company in a good way and with my integrity intact, which is so important to me. It's what I've built my long career on in the pharmaceutical/biotech world. I just felt it was time to pursue something I'd always wanted to do - set up my own virtual drug development company.

I'd always thought about starting my own company and it was my biotech training that convinced me I could do it, I'd shown that I could basically do everything virtually. So I thought, 'Right' I had one of those entrepreneurial postictal seizures, which I thought, 'Right, Tom, its time.' And, I formed my own company and I was doing very well initially, but along came the whole financial crash of 2007/2008. Around that time I had some financial support, I had the chance of compounds from Merck, I had things moving forward and then, all of a sudden, 2008 hit me. The NYC Investment Bank I was working with closed down, like many financial institutes in NYC and around the world.

**TT: And you were still in the States?**

TB: Yes, I was still in the States. So we struggled on, Jacqui and I loved our time in the States. The girls loved popping across, but I was starting to use my 401(k) plan (a US pension plan) to survive, various things like that, and then Jenny was having a baby in the UK, and we decided to come back in 2011. So since then I've just been doing lots other fun things, some consultancy, I consulted for a company in France and in the UK. I'm writing book chapters and a textbook on pharmacology for chemists with Terry Kenakin and Ray Hill. I'm lecturing and examining at UK Universities, and I'm sitting here talking to you about my life! What else is there?

**TT: Can I just ask, there's one thing you didn't mention, and that's teaching. You were an Adjunct Professor at one time?**

TB: Oh yes, at Steven's Institute in Hoboken, New Jersey, which is a very interesting institute actually. It's one of the oldest universities in the States, and it was built on an engineering tradition. However, they've developed programmes around bio-engineering/biotechnology and manufacturing. I was teaching biotechnology: how to make vaccines and monoclonal antibody development to students from US and India.

**TT: So were you teaching undergraduates or postgraduates?**

TB: Well, they were all postgraduate pharmacy students on the Masters course, I was teaching. Unfortunately, their English and essays were not always up to standard. And some had sent in course work from other students work from all around the world! They had a good plagiarism network...

**TT: I was once told off by my professor, I was a postdoc at St. Thomas', that it was not my business to correct students' grammar and spelling. Hang on, these kids are going to be prescribing drugs. It's important they know how to spell.**

**It would be really useful if we can talk about the influence of professional societies. The BPS is an obvious one. When did you become a member?**

TB: Oh, I think it was in the early 70s, well before I'd left ICI Pharmaceuticals. I think I must have been a member for about 40 years I think? At ICI, people like Professor Barry Cox and Dr Mick Turnbull and Desmond Fitzgerald were very much involved in the BPS, and it was a highly regarded society at ICI. So as a young guy, young pharmacologist, I basically enjoyed going to the meetings and I was in awe of these wonderful professors who used to sit on the front bench and ask you all these very difficult questions, and sometimes a very nice question that you could answer! And it was a great learning, training experience for me. To be able to stand up and give a presentation in 10 minutes and have roughly 5 minutes of questioning, from very eminent pharmacologists in the academic and the pharmaceutical world was quite a challenge. So it was tremendous training, and I used to enjoy those oral and poster presentations. There was one oral presentation in Dublin, which was my first presentation, and I was the last one on the Friday afternoon to present with hardly anyone in the lecture theatre. The professor (Philip Bradley) who was chairing the session had fallen asleep, not because of my presentation, but because of, I think, the excellent dinner and wine the evening before. And, I had one question from Professor Gordon Arbuthnott from Edinburgh, which was one I could answer.

**TT: Was that on the 6-hydroxydopamine rotational model?**

TB: Yes, that was on the 6-hydroxydopamine rotational model, a model you worked on Tilli. I also enjoyed, and still do, the BPS poster sessions in particular, because when you were presenting a poster or not, there were all these different posters topics and ideas around you. So you could be presenting a poster on say 5-HT research, and next to you could be a poster outside your field, say, on the activity drugs that acted on earthworms! For example, the anthelmintic avermectin or other fascinating research areas outside of your field. And then you'd have an idea to take back to the lab. It would spark another idea off and you'd say, 'I

wonder if I could apply that to my research?' Not necessarily earthworms! But, that drug or a technique or that statistical way of evaluating may be applicable to your research. The interaction and networking that goes on is so much part of, as you well know the BPS, and still is very strong within the Society. You can see that passion of the young investigators and the enthusiasm with regard to presenting their work. Now, those young investigators look at me as being one of those old guys asking the questions on the front row or at their poster. Whether they used the wrong statistics or if they use this drug instead of that drug? Why is it so important to use the rodent and not? So these aspects still inspire me, especially with regard to the BPS, or any scientific society.

**TT: You became the Meetings Secretary? That can be quite onerous?**

TB: Yes, very, as you come across all kinds of different people, egos and whatever. In those days I was fortunate in many ways, a number of people took me under their wing, people like Professors Bill Bowman, John Vane, Geoff Woodruff and Tony Birmingham, all people who I admired very much, with so many others. It was Professor Norman (Norm) Bowery who I worked very closely with over the years before and during my tenure as Honorary Meetings Secretary (four year post), Honorary General Secretary (two year post) and President. Norman really helped me and took me along with regard to some of the workings of the BPS, when I started to help out, as chair sessions, a poster referee, all of the other things that went with organising a large scientific meeting. May be because of my enthusiasm for the society, or some other reason, the BPS committee put my name forward to become Honorary Meetings Secretary. This must have been 1994/95, and this was the time when we had four meetings a year, three of them in universities, so that was the spring, summer and an autumn meeting. Then the big winter meeting before Christmas, which was generally held at a conference centre or a big hotel in the UK. For example, the Harrogate and Brighton conference centres. Norman had done a lot of the initial work with the Brighton Convention Centre, and we got some very good deals on hotel accommodation and use of facilities and audio visual aids.

In fact, when I go to any conference now the first thing I do, is look at all the audio visual facilities etc., to see how good they are and if I could do better. So that's still in my blood. It was such a privilege and an honour to be part of the BPS activities and still is (I'm now Chair of the Industry Sub-Committee for the next two years). In the sense that I was visiting all of the top universities in the UK, and abroad in Europe and America. I held a joint meeting with the American Society in San Diego and Dr Paul Insel, whose brother Tom Insel is now Head of NIH [National Institutes of Health]. I worked with ASPET [American Society for Pharmacology and Experimental Therapeutics] very closely and we had a very successful meeting there, with one little caveat: the Americans couldn't get their head around this 'Honorary General Secretary' title, and unfortunately there was some amusement at this name.

So when I became Honorary General Secretary, with Dr Nigel Baber from the clinical section, we decided to look at SWOT analysis; of the Strengths, the Weaknesses, the Opportunities, the Threat to the Society moving forward, for possible revenue issues for the journals, like open access publishing, and other matters that were possible concerns for the Society. Such as the membership and the number of pharmacology departments closing in the university system. We held a strategic workshop and looked at all aspects of the society's activities, and one of the proposals was to change the name of society officials to be in line with our sister organisations. So instead of having an Honorary General Secretary, we now have a President and Vice President of meetings etc. So I'm the only person now who, for one year, was Honorary General Secretary and the following year, President of the Society. It was one of the most fun times of my life, one of the most hardworking times in the sense of balancing the day job and the honorary position, which did at times bring me into some conflict with my employer.

**TT: This is when you were still at Beecham?**

TB: No, it was SB management at that time, who questioned how much time I was spending on BPS activities. However, all of the days and all of the time for BPS meetings I'd taken off as holidays, so for the summer/spring meeting, that was all taken out of my own personal time. But, that was never an issue with

me, as I was meeting so many wonderful people/scientist from all over this country, Europe, America. I set up the joint BPS meeting with the Australian Society before I left SB. It was a wonderful time in my life.

**TT: When you say you set up a meeting, that wasn't IUPHAR [International Union of Pharmacology] was it? Because that was earlier, wasn't it?**

TB: No, that was a joint meeting between the Australian Society and the British Society. Unfortunately I'd moved to the States when it was held, I'd set that up with Professor Jim Angus, it was in Melbourne and I'd moved to the States then, so I didn't get to go to that meeting. As they do now, we had to plan meetings four years in advance, to get the facilities booked and all of the preparation. But I had a wonderful team to support me during my terms of office. Sarah-Jane Stag (Executive Officer, Secretary) who then would be the equivalent of Jono Brüün today, but without the CEO title. Sarah-Jane was an amazing administrator; her previous senior civil service background made her an ideal person for the Society in managing policy politics and some of the rather large egos within the Society. Pam Dale, who was my right hand and left hand in organising the meeting with me - a fun person to work with. And lovely Michelle O'Gorman who was the Treasurer/Members Secretary of the Society. I had a great time and it was a great privilege working with them. Now we have a very young, dynamic team and the CEO, Jonathan Brüün, he is doing great things with the Society. We have one big meeting a year which is called 'Pharmacology 15', '16', '17' etc. And there are several other satellites like the Sir James Black Meeting and various other specialist meetings up and down the country. The Society's in good financial shape, with a very good team in the office and is moving forward with the times.

**TT: What kind of upset did it cause with you leaving, effectively a year early?**

TB: Yes, well some people were annoyed with me but you know essentially if you have a new job, you have to move with that job. Or if there's a chance of you losing your job, then you have to move on. But most people were very supportive and Norman Bowery was still very much involved with the Society. He took over for that year, for my final year.

**TT: Did you then join the American Society?**

TB: Yes, yes, I did for a while, but their meetings always fell at a very awkward time. I couldn't get to all of the meetings because it was always on my birthday, on the 24<sup>th</sup> April, and that time also fell in with Board meetings at work, with various other things, which I could never abandon! I think I went to about three or four of the meetings, and they got me to review posters.

**TT: Did you encourage people in your lab to join the societies?**

TB: Oh, absolutely. Particularly the young people.

**TT: Because you know the American Society banned anyone involved with commercial organisations until the 1940s. So I wondered whether you didn't join?**

TB: But, I did. Yes, well, but at the time when I was Meetings Secretary, we had a few internal issues with Glaxo using the BPS to fly their new compound, the anti-migraine compound. So there was a lot of internal discussion with regard to that.

**TT: I'm sure Glaxo weren't the only ones?**

TB: Oh no, no, but there again, you know, this point has come up again recently. I'm Chair of the BPS Industrial Committee now, and that's a two year tenure. I'm hosting a dinner in London in May for all the leading lights in the industry. We've invited Patrick Valance and several other luminaries, to sit down with them, tell them what we've been doing, what initiatives, what new plans we've got, and see how we can work with

them. Now whether that sponsors prizes, or whatever, although we've already so many prizes to present, it takes such a long time to get through.

**TT: I've been a couple of times as a guest to BPS dinners at the winter meetings as a humble member of Phys Soc; we have about five prizes. At the winter dinner it's prizes, prizes, prizes. And anybody who is doing clinical pharmacology gets a prize. It's deeply impressive.**

TB: Yes, yes. And now we've have 'The Drug Discovery of the Year Prize'. So we now pick a 'drug of the year', which the Industry Committee think is going to have a tremendous therapeutic impact.

**TT: Moving back to your own career, could I just ask you to elaborate a little bit about pressure about being innovative compared with doing generics work. You did mention that. Have you ever felt under pressure to get something slightly different?**

TB: I think there was a period within the industry where everybody was a lemming. They were all falling off the same cliff with regard to, me too, or fast follower, or whatever you like to call it. Paroxetine is an example of that in the sense that we weren't the first SSRI by any means, but the company made billions from it. So it's like every product we deal with in life, there are lookalikes, similar products, bioequivalents, whatever, and it's your market share that is the goal. You're seeing companies today now exchanging franchises in vaccines, basically to build their strengths around vaccines, and giving away some part of their empire which perhaps in another company would build that company franchise to differentiate themselves from the pack.

**TT: Have you found much difference going into the different companies and their corporate identity, their corporate policies, or have you chosen very carefully companies that would fit you? To begin with, where has the fit come, before, and/or afterwards?**

TB: No, the fit comes beforehand in the sense that I look at the people, I look to see if those people inspire me. Will those people take me to another level? And how much respect I have for them and their science. I think once you lose the respect for the people you're working with, I think then is the time to move on. When the people in the coffee room are grumbling about this, that and the other matters, you don't want to be in a coffee room with grumbling people.

**TT: What about personal ethics and integrity. Is that something you've carried with you all through your life and career, or has it been reinforced by particular people?**

TB: I really don't like anything associated with abuse, fraud or lack of integrity. We see so much of it in our lives where people are being taken advantage of, and I think that is something that has always been a very strong part of my DNA, particularly in the pharmaceutical industry, because that's where my passion has been for so many years. But when I read or hear or see or have possibly been subjected to poor decision-making, I quickly walk away and don't want to have anything to do with. Particularly when you're dealing with human life and medicines. We've seen some really crazy stuff recently with this guy in the States charging 5,000 times the value of a very old drug, less which you can make for fifty cents. That's the obscene side of my industry. These people are essentially committing fraud and taking advantage of sick people who perhaps don't know any better, and who trust these people/companies.

**TT: I think it's particularly difficult with medicine. You're automatically dealing with vulnerable people.**

TB: Very much so, yes.

**TT: Do you think that at any stage you actually felt yourself really driven to, or at any stage, at what stage did you feel you really wanted to make a difference, discover a drug, facilitate a drug?**

TB: Oh, very early on. Very early on. Even the days with R A Gregory, I was so excited, to see an experiment work and see if that experiment could lead to a new therapy. So it's always been with me, either reading something or hearing recently about a study in Seattle that is going to revolutionise the treatment of blood cancers, or going back to my early days and curing chickens of infectious bronchitis!

**TT: Have you ever been aware of any tensions between academia and industry?**

TB: Not really. Well throughout my career I've seen a lot of academics come into industry. Some have made it, some haven't. I've seen industry people move into academia, some have made it, some haven't. I think it's all about the people in charge and how they interact. Has that person got the leadership ability? Is that person innovative enough? Is that person willing to give you half a yard so you can take the project to the next stage? Within industry, you see people like Bob Ruffolo at SB, he was certainly one of those people in that sense, he told me one time, 'Tom, what I like to do is have a number of different projects all at different stages, and you try to seed them all, so that one or more are growing, which could be next year's project or the year after's project, while you're putting all your money into the main project.' But how you do that? It's like a manager of any business or in sports. You have to have the right people with the talent and who can see talent, who can nurture talent and who can bring that talent on, whether it's on a football field, academia or in the industry. Sometimes they don't see or want to see that, then they become battlefield fodder and they disappear before they've even had a chance to excel.

And I think that's a shame when you basically can destroy people's ambitions and dreams very quickly. I think sometimes, there's the old adage about management and pulling up the plants to see the roots grow. You know that's not good but it's the world we live in now, that's what we're doing more of. There's no doubt about it, we're very accountant driven now. Ever since the Sarbanes- Oxley Act that came into force the US in 2002. This is the legislation imposed public company accounting practices to report every quarter. So you know you're project/company is under scrutiny more and more every quarter, because of what went on with Enron and other companies. That's what some say is what is happening to science, academia and the industry. We're not getting the creativity perhaps, or we can't afford to let the creativity move forward as we once did in the past.

**TT: One of the points that was raised in the 5-HT Witness seminar, in the migraine meeting and others, was how universities have got so obsessed with their own intellectual property [IP]. This is especially when people talk about collaborations in the 80s and 90s, and they say 'Of course it couldn't happen now.'**

TB: Don't get me started.

**TT: I would like to get you a bit started. What's your take on this?**

TB: Well, one of the reasons why I set my business up in the States was basically I could see both within the industry, and certainly in academia, where compounds, medical devices were not being moved forward quickly enough because of internal/external issues, whether that be finance, market size, competition, IP or whatever. There are so many different factors. I started to go into universities in the US and talk to them, I went to John Hopkins, Harvard, Columbia, talking to these universities about spinning out and providing them with development skills and money through various financial institutions, whether it be non-profit or VC sources. And, to accelerate the development their IP assets, which is very much like the many stalled projects within the industry. The industry is very good initiating projects and the discovery novel compounds, but not all the projects survive. They can't take all those compounds forward, because like any industry they have fixed budget each year. Which is being reduced every year now. When I started my career in the 70s, to develop a new medicine would cost around \$50 million. Now it's more like \$2 billion. So in that timeframe, 46 years, it's become far too expensive even for Big Pharma to take more than one project forward per year.

So universities and pharma have a sustainability problem often as they can't afford to support, maintain their intellectual property because of increasing costs. So, therefore, there's a lot of intellectual property unsupported and disappearing with people's ideas and people's dreams, because the intellectual property will never see the light of day in a novel drug or product. For example, I worked with a big pharma company for four years trying to out-license one of their IP assets, and worked with four different Business Development guys, all to no avail. Another example. I went to one university in this country, to do a SWOT analysis of this very eminent scientist's intellectual property, and how he was taking it forward. Basically, it was like our *TIPS* guy with his 101 indications. But when you asked the question, 'Where's your next grant coming from?' 'Oh, the MRC or Wellcome.' 'But where's it coming from after that?' 'Well it doesn't matter.' 'Oh yes it does.' Because to take those projects forward they've got to be viable, it has to be a sustainable business model that you actually show you're moving forward. So it's okay to say, 'Oh, I've found this other indication' but what you need to do with any drug in the industry, academia or wherever, is to get that first study in man that shows some efficacy/safety. And once you've got that first study you can then attract more finance, then you can start to elaborate about other indications or you can actually build on that one study and make it into the sort of blockbuster drug that the industry needs for their survival. It's the age of collaboration now between all parties to develop new much needed drugs.

**TT: I think you're giving us a master class in innovation as well as oral history, Tom. Thank you very much for your time.**

[END OF TRANSCRIPT]

**Further related resources:**

1. Overy C, Tansey E M (eds) (2013) *Drugs Affecting 5-HT Systems*. Wellcome Witnesses to Contemporary Medicine, vol. 47. London: Queen Mary, University of London.
2. Overy C, Tansey E M (eds) (2014) *Migraine: Diagnosis, treatment and understanding c.1960-2010*. Wellcome Witnesses to Contemporary Medicine, vol. 49. London: Queen Mary, University of London.
3. Tansey E M (intvr); Tansey E M, Zarros A (eds) (2016) *Blackburn, Tom: transcript of a video interview (22-Feb-2016)*. History of Modern Biomedicine Interviews (Digital Collection), item e2016046. London: Queen Mary University of London.