

# Fatima Cardoso: the next generation

→ Marc Beishon

Fatima Cardoso's determination to put her considerable abilities to best use landed her the scientific directorship of a groundbreaking translational research trial at the tender age of 37. A founder of the Flims Alumni Club, she's now calling on other budding young researchers not to wait until they become the big shots, but to make their voices heard now.

**M**ost people entering a medical career want to make a difference – and the choice of oncology is often made because of the potential to contribute to this most problematic disease management area. While it is possible to make a steady contribution in day to day treatment work, the ideal, perhaps, is to be part of an exciting research group as well as a good clinical physician – which is exactly what Fatima Cardoso, assistant professor at the Jules Bordet Institute's medical oncology clinic in Brussels, has achieved.

But in doing so she's encountered nearly all the major issues affecting oncology work in the European Union, such as mobility, career paths and research funding – obstacles that some other colleagues in her home country, Portugal, have found too tough to crack.

As a relatively young medical oncologist, still working on her PhD, Cardoso is already the scientific director of TRANSBIG, the translational research network spun out of the Breast International Group (BIG). TRANSBIG's first

project – MINDACT (Microarray for Node Negative Disease may Avoid Chemotherapy) – involves a major trial with 6,000 patients that promises to make a significant difference in determining which women with early breast cancer will benefit from chemotherapy. "It's almost like science fiction," she says of its potential.

Running a project of this size is certainly giving Cardoso her cutting edge research ideal, but as she points out, this sort of translational work requires expertise and oversight in both clinic and the laboratory, and she welcomes the chance to keep a foot in both camps. "I have learnt that for me to be fulfilled as a doctor I need to have enough time to see patients," she says. Cardoso loves the opportunities working at Jules Bordet offers to immerse herself in bringing together the worlds of lab and clinic, seeing patients every day, working on many of the 100 trials currently running, participating in the projects of the institute's translational research unit, and pressing on with MINDACT and her own research into Herceptin (trastuzumab) resistance.



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## Cardoso hopes younger oncologists will help speed up recognition of medical oncology as a speciality

She's climbed very high for someone of her years, but Cardoso is not one to pull the ladder up behind her. She cofounded and enthusiastically promotes the Flims Alumni Club (FAC), which brings together young graduates of the highly respected Flims Methods in Clinical Cancer Research Workshop. At the Jules Bordet, she has also taken on the role of coordinator of the community of international fellows, which until recently she herself was a part of. Such networking, says Cardoso, is not just about learning how to run trials, for example. "It's also about making our voice heard now and not waiting until we're the big shots. We need to say now what we want for our careers."

There can certainly be frustration for younger cancer doctors in pursuing their goals, especially when, like Cardoso, they determine their interests fairly early on. The situation is particularly acute in Portugal, she says, because while standards of clinical care are high, the medical training is very long and there is simply very little research infrastructure. "I had my medical training at the University of Oporto, which is considered to have one of the highest standards of theoretical learning in Europe. But what is missing is the research infrastructure – you have to do everything yourself and you simply don't have the time with clinics so full." There is an excellent private research institute (IPATIMUP) in Oporto, she adds – known particularly for work on thyroid cancer – "But working there takes you away from patient care."

Cardoso's aim to be a doctor stems from her early years. She was born in Mozambique. Her parents – mother a teacher, father an insurance business manager – had moved to the Portuguese colony, but had to return when Fatima was eight after the political upheavals. "I never wanted to be anything other than a doctor – my mother says that ever since I was little

I was always playing doctors and my family had to pretend to be sick all the time."

When she became aware of medical specialities, her first choice when she arrived at medical school was to go into paediatrics, but a bit later she decided against, feeling it would be too hard in emotional terms. "I'm a very sensitive person – it especially hurts to see a child suffer. I believe that to be a good doctor you need to keep your humanity. People say that you have to keep your distance otherwise you'll get hurt all the time. But if you do that you lose your quality as a doctor. I felt it was easier for me to be able to keep my humanity, without being overwhelmed with pain, with adults than with children."

She chose internal medicine over an option to become a surgeon. "I realised I wouldn't be happy as a surgeon – no disrespect, but I'd be doing the same things over again and I would be bored. That may be a misconception but it was the way I saw it.

"And I'd discovered oncology, first through theory – cancer biology became a passion as soon as I encountered it – and then medical oncology became a speciality the year before I had to decide." To its credit, Portugal has moved faster than some other countries to recognise medical oncology, and it is certainly Cardoso's hope that younger oncologists will help accelerate the process of breaking open other national internal medicine systems to this core speciality.

She also benefited from excellent and inspirational teaching, and found added impetus in her personal life, especially from her sister, who had been through many operations after a childhood accident. "She's my role model in terms of courage and not letting things stand in your way – she's a robotics engineer now and I'm very proud of her." Then her best friend was diagnosed with breast cancer. "When you are young you have all these dreams. I thought if I worked hard and in the right team I could do something

to make a difference in cancer management, and eventually help my friend. It's why I went into medical oncology and one of the reasons I left Portugal to come to Brussels."

Despite Portugal having three regional cancer centres, Cardoso had found research opportunities, at Oporto at least, very limited. Such research as she was able to do was done in the evenings and weekends, and she was encouraged by her director to seek opportunities abroad. After 12 years in training – Portugal is said to have the longest medical qualifying time in Europe – she actually put in only three months as a fully-fledged medical oncologist in Oporto.

"We had a speaker from the Jules Bordet breast unit come to a meeting, and in the coffee break my director asked him if I could do a research project in Brussels, and I thought, 'Well, you could have asked me first!'" That was in 2000, and Cardoso duly took up an offer to become a fellow at Jules Bordet. She is now a staff member, and very grateful to her former director for his 'push'. As she points out, being single with no ties has made the move easier, and she already spoke French and English.

As for leaving Portugal, she admits that she's contributing to the 'brain drain' – a hotly debated issue in Portugal as in other countries. However, she debunks the idea that she is somehow in debt for the cost of her training. "The money spent on my training I've paid back in the long hours I worked as a resident. You can consider that it was cheap labour. I always gave my best and a lot of my time." While proud to be Portuguese, she says that its society needs to tackle some tough issues. People tend to look out just for themselves, she says, adding that this may well be a reaction to the long years of dictatorship. Those such as doctors who stay within public positions have continually to 'fight the system' to get professional fulfilment.

At Jules Bordet, Cardoso first completed a two-year clinical and translational research fel-



With her guide and mentor  
Martine Piccart

lowship, where her focus on breast cancer was cemented. This was a crucial stage of her career, which she saw as a natural progression from her interest in targeted therapies. It also presented a wonderful opportunity to work with one of Europe's leading breast cancer groups, under the direction of Martine Piccart, who founded BIG in 1996, and who has been her guiding force over the last few years. And in a profession still heavily dominated by men, Cardoso feels that working for such a successful woman has helped pave the way for her own career.

More generally, with its heavy emphasis on multidisciplinary working across the clinical-laboratory divide, and given the many breast cancer patients referred to the Institute,

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In the lab

Cardoso saw Jules Bordet as an ideal place for her to pursue her key research interest – the fundamental puzzle of why targeted therapies fail in such a high percentage of cases.

“There are people who prefer to go into areas that are not as well studied as breast cancer, so if they discover something it becomes their breakthrough,” she says. “Others go into areas where there are many groups studying variations on a theme, and where there is much more collaboration – although honestly I didn’t think of one or the other.” Nevertheless, it has since become abundantly apparent to Cardoso that there are tremendous advantages in the power of large-scale collaboration, such as that fostered by BIG. Typically modest, her wish is to play a part and not to see her name in lights.

While her PhD is on trastuzumab resistance, she adds that it is the overall problem of treatment resistance that is her major topic – the mechanisms and predictive markers. To develop her translational research capability, on completing her two-year fellowship she went to the MD Anderson Center in the US on a one-year basic research fellowship under Mien-Chie

Hung, head of breast cancer research and a pioneer in HER-2 science. This, she says, was for the very specific aim of finding out more about basic research, and she feels a year was sufficient. “I could also have gone to the UK and the University of Oxford, but I would have had to put in three years instead.”

Several ‘lessons’ emerged from this spell at MD Anderson. “It reinforced my understanding that I had to also work with patients, which you don’t do in basic research,” she says. “But the main lesson was finding out exactly how people in the lab think – it is different from those on the clinical side, where we need to know why we are doing something. In the lab they are usually doing science for science’s sake.”

Another lesson came the hard way – you can go into the lab with a hypothesis and test it out, but if it doesn’t work then some six months or so of the experience can be wasted, at least as far as getting a usable result is concerned. That’s clearly a potential risk of spending only a short spell in the lab environment, but as Cardoso adds, it brings home the importance of knowing what has already been tried and failed.

“I believe it’s unfortunate that we are much more likely to publish – and have accepted for publication – work with positive results. That’s perhaps even more striking in clinical research than lab work. It’s a bias that should change – we should be able to publish negative results so other people don’t waste time investigating the same dead ends.”

What’s more, she feels that without more publication of negative results, the oncology community is getting a biased view of research. “I guarantee that if you do a search on MEDLINE more than 90% of papers will have positive results.” It’s a situation that is changing though – Cardoso mentions one drug study she’s recently reviewed, in the breast cancer area, which has a negative result and will be

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published. “It’s a well-written paper and it should be known that that specific drug given this way doesn’t work.”

It’s another item to add to her change agenda for the oncology community, though she notes that all are to blame in the natural desire to be associated with positive outcomes. “In breast cancer, though, we are talking about this. I’ve found sessions where we discuss how to get manuscripts accepted very interesting, and editors and opinion leaders are aware of the issue.” In addition, she feels that the breast cancer research community is more organised and open to collaboration, so enhancing protocol power and the chances of positive outcomes.

From MD Anderson, Cardoso was taken onto the staff at Jules Bordet, but she had to complete a year of internal medicine and sit an exam before being accepted as a practising medical oncologist. This was a disappointment. “It is duplication of effort and not really fair, as if you look at my CV it’s exactly the same as a qualified Belgian medical oncologist,” she says. “I can understand it if you come from a country where your training is a few years less – you must demand that a person is competent. But we need to make procedures much more homogeneous throughout the EU, otherwise the free movement of people is not a practical reality, just a dream.”

At Jules Bordet, there has been an improvement – extra accreditation for some colleagues has reduced from a maximum of three years down to immediate acceptance in one case. But as Cardoso says, the situation is likely to be inconsistent across other cancer centres in the EU.

Cardoso was in at the beginning of the TRANSBIG project in 2002. It builds on the collaborative power of the structure developed in BIG and moves the agenda from the clinical to the translational arena. As she notes, “Most people working, for instance, on predictive

markers have been doing small studies, which despite being important, do not have enough power to provide definite conclusions. However, to do such a large trial as MINDACT requires a huge amount of money.”

MINDACT, she explains, is the first of a new generation of large-scale trials, and is using the new microarray technology to classify node-negative early breast cancer patients into high and low risk of relapse, and compare them with traditional clinical assessment. The project uses the 70-gene prognostic signature developed at the Netherlands Cancer Institute, and the clinical side of the trial is being coordinated by the European Organisation for the Research and Treatment of Cancer (EORTC).

As scientific director, Cardoso manages the network of 39 partners – clinicians, lab technicians, statisticians, and bioinformatics specialists among them. “This is why my training at MD Anderson is so important. I feel like a translator between one world and another.” It’s a big logistical challenge, particularly as the microarray technique requires fresh tumour samples to be sent to Amsterdam. “Patients are operated on, the sample is sent the same week, and within a maximum of 15 days we must have the full pathology report and the results from Amsterdam,” she says.

For this first TRANSBIG project, Cardoso has been Martine Piccart’s ‘right-hand person’. Her involvement has gone way beyond the fieldwork, to writing grant applications for the estimated 35mn euro funding that’s needed. She also plays a leading role in helping to publicise the trial. She was surprised to find that despite BIG’s success at now running some 20 worldwide clinical trials, it has been a struggle to obtain national or European Union funding. The EU is partially funding MINDACT, but has only given 7.5mn euros, and thanks to arcane rules, would only finance a new organisational



With her mother and sister Xana (right). Xana's courage in facing down obstacles after a serious childhood accident has been an inspiration to Fatima

structure and not the trial itself – necessitating the creation of TRANSBIG out of BIG. Two other TRANSBIG projects submitted to the European Commission, a microarray radiotherapy trial and a project aimed at older patients, had their funding requests rejected on the grounds they were “too ambitious” and have consequently had to take a back seat. The priority now is to court other funders for MINDACT.

In addition to all the discussions to do with funding applications, Cardoso has also had to tackle the thorny issues of intellectual property rights, the involvement of commercial interests (as part of EU rules), and ethical issues. “It’s been interesting to see the other side of clinical trials,” she says. “I imagined myself as just an investigator putting patients through trials, which is already a lot of work, but all these other legal, ethical and financial aspects have been a roller coaster of a learning curve.”

One requirement of EU funding that Cardoso has welcomed is the obligation to provide information about such trials that can be understood by a lay audience. The MINDACT/TRANSBIG descriptions are almost a

model in science communication, and Cardoso says they will be producing a patient package, perhaps with a video. She feels there is an acute need to promote wider understanding of clinical trials in general, to address the lamentably low participation rate even in the best centres, and she comments that media coverage on the ‘controversy’ of mammography, in particular, upsets her greatly.

It’s all experience that she can feed back to other young researchers via the Flims Alumni Club, where she has already served two terms as vice-president, and the Flims clinical cancer research workshops, where she is now part of the faculty. “You go on the course with an idea for a protocol and learn how to write it in a week – it would normally take months.” About 60–70 young oncologists a year now attend the workshop in Europe, with similar initiatives running in the US and Australia. “It was an important experience for me and for 99% of people who do it – it touches your career from then on.”

The Alumni Club came about, she says, because “a group of us decided we didn’t want to lose touch – young people who learn the basics of research should be kept together. So we thought about creating a society that would set up a network of young researchers across the board – not just clinicians, but scientists from other disciplines. It’s evolved nicely and we are now a member of FECS [Federation of European Cancer Societies], which has given us great support.”

The multidisciplinary nature of the Alumni Club, says Cardoso, is a feature members see as a key message for others “We want the societies to talk more to each other instead of infighting because our goal is the same. We wanted to set an example – yes, we are young and yes we still want our own societies, but we can also work in multidisciplinary groups. Perhaps our generation

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can be the one that really works together.” She’s happy to report that alumni members are already appearing on journal boards and various steering committees.

She adds that her own grouping, the powerful ESMO (European Society of Medical Oncologists), “must admit they can’t fight cancer alone.” But while the friction between professionals is perhaps most apparent at the society level, Cardoso feels that much of the problem stems from the very start of medical training. “The way you move up your career doesn’t facilitate communication. Medicine is an extremely competitive world and it starts in medical school.

You’re taught even before then that you have to be the best to get in and it’s put into your head that if you want to continue on top you don’t open your game to everybody. I know whenever I was second best in training I was extremely sad and disappointed.”

Second best Cardoso certainly isn’t – her medical oncology residency at Oporto was marked at 19.3/20 and in Belgium she earned a high distinction from the Free University in internal medicine and also an oncology masters (the highest distinction). “Only the best get the grants and go on getting funding – it’s the way the system works. But living and working in such a highly competitive world, you lose a bit of your idealism.”

While competitiveness for scarce resources is hardly unique to medicine, there is also an element of working the system and luck with opportunities. As she says, “I’ve known very good people who’ve been overwhelmed with clinical work and given up research. If I’d stayed in Oporto I would probably have done the same – you run out of steam at some point.”

When we interviewed Cardoso, it was at the end of a particularly difficult week that tested her idealism to the full. “I lost four patients this



week – it’s not a good time to ask me why I chose oncology. It’s so hard to tell a young girl her mother is going to die in a few days. I don’t want to lose my desire to put myself in the patient’s shoes, but it’s not easy. But when I see someone I know is going to die I know I’m doing something to avoid such deaths in the future.”

Since coming to Belgium, Cardoso has been pretty much immersed in oncology. “My family say I’m married to medicine, but I do have other interests. I love music, and also computers – I teach myself about them and have a laptop with me wherever I go. I’m a bit of a geek I guess.” She also writes poetry – as this is in Portuguese, we won’t attempt a translation here. Apart from family and friends, she misses being by the ocean – “The North Sea is not the Atlantic” – and her dream country to live and work in is Australia.

While such thoughts suggest a future move, TRANSBIG, her research and the Brussels clinic are the priority. Expect to see her name on a seminal paper on the MINDACT protocol fairly soon – and the longer the list of co-authors, the happier she’ll be.

*Thanks for your help! Cardoso with her fellow vice-president of the Flims Alumni Club Vanesa Gregorc (left) present the veteran French oncologist Jean-Pierre Armand with the first FAC Award for Exceptional Support, 2003. Behind them stand the current president Razvan Popescu and past president Jean-Charles Soria*

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