Career Workshop for Young Medical Mycologists

The post-doc to PI transition – the truth, the whole truth, and nothing but the (ugly) truth

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A couple of disclaimers before we begin...

The views and opinions presented in this talk are solely those of Dr. Quinn. They **DO NOT** represent the opinions of:

- The Wellcome Trust,
- or Newcastle University...

Only ~10% of post-docs will go on to start their own labs, so honesty is the best policy.
Luck is absolutely required (but you can help luck along...)

1) Work for PIs that publish a lot (publications are academic currency)

2) Work for PIs that are leaders (or strong potential future leaders) in their research fields (“state of the art”)

3) Work your butt off (your competitors are; and think about “probabilities”)

4) Write all your own stuff (publications are academic currency)
1991-1994 PhD studentship
Autoantigens in Primary Biliary Cirrhosis
Lipoylated and unlipoylated domains of human PDC-E2 as autoantigens in primary biliary cirrhosis: significance of lipoate attachment.

Quinn J, Diamond AG, Palmer JM, Bassendine MF, James OF, Yeaman SJ.

Hepatology (1993) 18, 1384-91

Department of Biochemistry and Genetics, Medical School, University of Newcastle upon Tyne, United Kingdom.

Abstract
1994-1997 Post-doc 1
Chromatin remodelling by the yeast SWI/SNF complex

Fellowships (USA)

HFSP Postdoctoral Fellowship (1995 - declined)

American Cancer Society (1995 - declined)

HFSP postdoctoral fellowships encourage early career scientists to broaden their research skills by moving into new areas of study while working in a new country.

The EMBO Long-Term Fellowships are awarded for a period of up to two years and support post-doctoral research visits to laboratories throughout Europe and the world*. International exchange is a key feature in the application process.

Sir Henry Wellcome Postdoctoral Fellowships This fellowship provides a unique opportunity for the most promising newly qualified postdoctoral researchers to make an early start in developing their independent research careers, working in the best laboratories in the UK and overseas.
Stimulation of GAL4 Derivative Binding to Nucleosomal DNA by the Yeast SWI/SNF Complex

Jacques Côté, Janet Quinn, Jerry L. Workman, Craig L. Peterson*

The SWI/SNF protein complex is required for the enhancement of transcription by many transcriptional activators in yeast. Here it is shown that the purified SWI/SNF complex is composed of 10 subunits and includes the SWI1, SWI2/SNF2, SWI3, SNF5, and SNF6 gene products. The complex exhibited DNA-stimulated adenosine triphosphatase (ATPase) activity, but lacked helicase activity. The SWI/SNF complex caused a 10- to 30-fold stimulation in the binding of GAL4 derivatives to nucleosomal DNA in a reaction that required adenosine triphosphate (ATP) hydrolysis but was activation domain-independent. Stimulation of GAL4 binding by the complex was abolished by a mutant SWI2 subunit, and was increased by the presence of a histone-binding protein, nucleoplasmin. A direct ATP-dependent interaction between the SWI/SNF complex and nucleosomal DNA was detected. These observations suggest that a primary role of the SWI/SNF complex is to promote activator binding to nucleosomal DNA.

The yeast SWI1, SWI2/SNF2, SWI3, SNF5, and SNF6 gene products are required for the induced expression of a large set of genes (1). Furthermore, SWI/SNF products are required for the enhancement of transcription by several gene-specific activator proteins in yeast, such as GAL4 (2), Drosophila fct (3), mammalian glucocorticoid

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and estrogen receptors (3), and LexA-GAL4 and LexA-Baculovirus fusion proteins (4). The SWI/SNF gene products function as compo-

6). One activity of this complex is to associate with the mammalian glucocorticoid receptor (3). These observations suggested that homologs of the SWI/SNF genes would be present in Drosophila and mammals (3). Candidate homologs of the SWI2 gene have been identified in Drosophila (7), mouse (8), and human (9, 10). Protein chimeras between either BRG1 (one of two putative human homologs) or brahma (ben, the putative Drosophila homolog) and SWI4 are functional in yeast, which suggests that these relatives are functional homologs (9, 11). Gel filtration data suggest that the BRG1 protein may also be a subunit of a large protein complex (9).

A current hypothesis of how the SWI/SNF complex facilitates activator function suggests that the complex antagonizes chromatin-mediated transcriptional repression. The relationship between the SWI/SNF complex and chromatin structure was suggested because mutations in genes that encode chromosomal proteins alleviate the phenotype of swi and snf mutants. Mutations that inactivate the SNF1 gene, which encodes histone H3, alleviate the defects in growth and in transcription caused by mutations in

Table 1. Purification of the SWI/SNF complex was followed by protein immunoblotting probing for the SWI3-HA-HIS5 fusion protein. Similar levels of purification were obtained in at least four preparations.

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<th>Volume</th>
<th>Concentration</th>
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<td>1.5</td>
<td>0.02</td>
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A unit is equivalent to the amount of SWI3-HA-HIS5 fusion protein in 100 μg of whole cell extract as measured by immunoblotting. The overall yield is estimated to be approximately 25 percent.

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DNA-binding properties of the yeast SWI/SNF complex

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The SWI/SNF complex is required for the enhancement of transcription by many transcriptional activators in yeast1,2. Genetic and biochemical studies indicate that the complex facilitates activator function by antagonizing chromatin-mediated transcriptional repression3,4. The absence of known DNA-binding motifs in several SWI/SNF subunits and the failure to identify SWI/SNF-dependent DNA-binding activities in crude yeast extracts have led to the belief that the complex does not bind DNA3. Here we show that the SWI/SNF complex has a high affinity for DNA and that its DNA-binding properties are similar to those of proteins containing HMG-box domains5. The complex interacts with the minor groove of the DNA helix, binds synthetic four-way junction DNA, and introduces positive supercoils into relaxed plasmid DNA. These properties are likely to be important in the remodelling of chromatin structure by the SWI/SNF complex.

A gel retardation assay was used to test whether the purified yeast SWI/SNF complex binds DNA. The data in Fig. 1 show that the SWI/SNF complex binds with high affinity to promoter sequences from both SWI-dependent (SUC2 and ADH1) and SWI-independent (CYC7) genes (Fig. 1a). Based on the concentration of SWI/SNF complex needed to bind half the probe DNA, we estimate the apparent binding constant to be 1.9 × 10^1 M
Professor Brian Morgan

'Mike if you don't become a PI after 2 postdocs it's never gonna happen'
Prof Craig Peterson 1995
Applying for independent positions

**Fellowships (UK)**

Royal Society University Research Fellow

**UNSUCCESSFUL**

Wellcome Trust Career Development Award

**UNSUCCESSFUL**

MRC Career Development Award - Invited for interview

**SUCCESSFUL 😊**

If at first you don’t succeed ...............
External Fellowships

Internal Fellowships

Apply directly for lectureship

External Fellowships
Career development award

Five years' support for outstanding post-doctoral researchers to make the transition from post-doctoral research trainee to independent investigator. It includes an option of 12 months research training outside the UK, in UK industry, or at another UK research centre, to enable fellows to acquire new transferable techniques and skills. (~10-15 pa)

The New Investigator Research Grant (NIRG) can provide talented early-career scientists with a route into a permanent lectureship position. For those who already have a post it provides funding and ‘protected time’ with which to establish an independent research career. A NIRG is also a potential source of research funding for fellows whose awards only cover a personal salary. Three years funding – 26 awarded 2011-12

Awards are for 5 years, up to 5 are available, and include personal salary and a significant research support grant.
University Research Fellowship

This scheme (5 years +) is for outstanding scientists in the UK who are in the early stages of their research career and have the potential to become leaders in their field. 35 pa

Sir Henry Dale Fellowship - in collaboration with the wellcome trust

For outstanding post-doctoral scientists (5 years +) wishing to build their own UK-based, independent research career addressing an important biomedical question.

Dorothy Hodgkin Fellowship

This scheme (5 years) is for excellent scientists in the UK at an early stage of their research career who require a flexible working pattern due to personal circumstances such as parenting or caring responsibilities or health issues. Female candidates are particularly invited to apply. 5 pa
What is the advantage of obtaining a UK Fellowship?

Academic freedom (5 years +) some with option to study abroad and get new skills

No teaching requirements

No administration requirements

Some provide post-doc support

Independent publications

Flexibility (£ follows you if you want to move)

Prestige
Independent Researcher Establishment Scheme (3 posts)

£27,578 rising to £44,166 (depending on experience)

The Institute for Cell and Molecular Biosciences (ICaMB) at Newcastle University:
- Is a world-leading and internationally recognised research Institute.
- Major recent awards include four European Research Council Advanced Grants, two Wellcome Trust Senior Investigator Awards and multiple programme grants from the MRC, BBSRC, LLR, Wellcome Trust and CRUK.

We are now looking to strengthen our research portfolio by appointing three Research Fellows under our new Independent Researcher Establishment Scheme (IRES). This is an exciting opportunity for early career scientists who aim to be research leaders of the future.

- You will be expected to establish an international reputation in your research area and to obtain independent funding during your IRES tenureship. Following a rigorous probationary assessment after three years, successful Fellows will be offered a permanent position in ICaMB at the a level to be determined by performance.
- In addition to a CV, candidates should attach a statement to their application, describing their research interests and their strategy for establishing an Independent career. This statement should also indicate how they expect to complement and extend our current research activities which can be found on our website:

  [http://www.ncl.ac.uk/camb/](http://www.ncl.ac.uk/camb/)

Online applications should be submitted at:- [http://www.ncl.ac.uk/vacancies/](http://www.ncl.ac.uk/vacancies/) using reference number A1432R

Closing date: 17 March 2013, with an interview date in April/May 2013

Informal inquiries can be made through:
Bob Lightowlers, Institute Director (robert.lightowlers@ncl.ac.uk)
Neil Perkins, Institute Fellowship Advisor (neil.perkins@ncl.ac.uk)
Lecturer in Biomedical Sciences
Brunel University - School of Health Sciences and Social Care
Vacancy Ref: BKA0106-2

Salary H3 scale: £36,389 - £46,773 per annum Incl. of London Weighting

The Division of Biosciences invites applications from scientists with a proven record of research achievements in any of the following areas: Molecular and cellular biology, Chromosomes biology; Cancer biology; Microbiology / Immunology and is able to deliver flexible relevant lecture topics in biosciences.

Applicants should hold a PhD and have extensive post-doctoral research experience. The successful candidate will be expected to develop a strong, externally funded, research programme and to participate in the administration and teaching of our BSc Biomedical Sciences and MSc Molecular Medicine degree courses.

Informal enquiries may be addressed to Division Director for Biosciences, Dr. Suling Li (Suling.Li@brunel.ac.uk).

Closing date for applications: 9 May 2013
Applying for independent positions - FAQs

Is it easier to get a PI position in the same place of the post-doc or more chances changing university-city-nation?

1) Usually better to move locations and establish independent research group, but...
   a) +VE → if you’re research area is specialized, maybe there is no place better to go!
   b) How do you work alongside your past advisor?
      i. Are they retiring? Or moving?
      ii. Did you start something VERY unique that your advisor isn't interested in?
      iii. Is there enough room for both of you?

What's the minimal CV (i.e. - publications) that is good enough to apply for a first PI position?

1) IF > 30 (e.g. - Cell/Nature/Science), go for it!
2) IF 8-15 (e.g. - Molecular Cell, Genes & Development, EMBO Journal, PNAS, PLoS Biology, PLoS Pathogens, Cell Host Microbe), very competitive
3) IF 5-8, (Mol Cell Biol, Mol Biol Cell, Mol Micro, J Biol Chem, EMBO Reports) if have several - competitive
4) IF < 5, it will be tough

REALITY CHECK - competitors probably have >1 IF=8 papers in CV ............but its also about being at the right place at the right time!!
How do you convince someone that your research is worth funding?

It’s no good having great ideas if you can’t write convincing fundable grant proposals.

- What helped me? Writing all my own papers & applying for post-doc fellowships.
What did/do you do when times are hard and you feel like giving up?

1) Understand that (almost) everyone goes through tough times, so you’re not alone.

2) Don’t lose perspective: you’re smart, you have a PhD, opportunities will present themselves.

3) Have a backup plan (or five). When applying for fellowships I considered....
   a) Further postdocs (... but note previous quote!)
   b) Editorial positions (another way to impact science)
   c) Educating the next generation (in a dream location)
2005-2008 Lecturer
2008- Reader in Molecular Biology

ONCE YOU GET THERE IS IT WORTH IT?

Cons:

Time at the bench ↓

Time teaching ↑

Time doing admin ↑

Time spent actively seeking (& worrying about maintaining) research funding so can run lab ↑↑↑
2005-2008 Lecturer
2008- Reader in Molecular Biology

ONCE YOU GET THERE IS IT WORTH IT?

Pros:

You get to do a job that isn’t work

Many great PhD students past & present

Grant funding = post-docs

More papers = raises profile in the field

Collaborations with great guys that are excited about the same stuff

Travel