comments

Quality of care is now being measured for many surgical procedures. The coronary bypass is probably the first surgical procedure to be investigated in depth because of its high profile. The more recent development is that 'perceived' quality is being translated into action by payers and consumers, either by selecting providers to participate in a programme or by an enhanced payment system. Pilot projects to reward 'quality' are being initiated by both private and governmental insurance programmes. In my opinion, the field of urology has lagged behind other surgical and medical specialities in addressing the quality issues of urological practice.

There are recent noteworthy articles in both the medical and lay press. In July 2003, Sternberg [1] suggested in an editorial that ". . . quality of care should be measured and reported routinely at both the national and provider-specific, i.e. hospital and physician levels." In *The Wall Street Journal* on March 25, 2004, an article described plans for a consortium of 28 large employers to develop 'score cards' to help employees to choose doctors, based on how well they care for patients and how cost-efficient they are. The Leapfrog Group, a coalition of public and private organizations that provides health care benefits (e.g. organizations ranging from the Board of Pensions of the Presbyterian Church, USA, to the Washington State Health Care Authority, to General Motors Corporation), has established standards for patient safety, and rewards providers or hospitals for best performances. Thus, there is no doubt that quality of care at both the hospital and individual physician level is going to be measured closely, and the resulting data will translate into higher payments for the best performers.

Unfortunately, there are still major gaps in knowledge about quality of care. Historically, the focus has been on disease-specific factors; in oncology this relates to tumour

QUALITY OF CARE IN UROLOGY

JAMES E. MONTIE – Department of Urology, University of Michigan, Ann Arbor, MI, USA

grade, pathological stage, etc., and treatment has often been based on single-institution retrospective experience. These studies have commonly ignored potentially modifiable clinical factors, structures and processes that are measured by their association with morbidity, mortality and length of stay (LOS). One of the recognized fathers of quality of care initiates, Avedis Donabedian, was a Professor of Public Health at the University of Michigan for many years. He described quality of care through three components, i.e. structure, process and outcomes [2]. Structure is related to the support from the system and includes hospital equipment and support, training of individual surgeons, and patient volume of an individual surgeon or hospital. Process, on the other hand, relates to the actual care provided and usually relies on evidence-based medicine (e.g. prophylaxis for deep vein thrombosis). Unfortunately, in urology there are few data on specific process measures that are known to make a difference. The most commonly used measure of quality is outcome, which is reflected by morbidity, complication rates, mortality rate, functional health outcomes commonly referred to now as 'quality-of-life assessments', patient satisfaction evaluations, and costs. Urologists have previously not approached quality from an *inclusive* viewpoint; unfortunately, they have often focused on one set of outcome measures, which are those most easily obtained from a retrospective chart analysis.

A good example to examine for quality of care in urology is a radical cystectomy for bladder cancer. The contemporary perioperative mortality and morbidity rates are substantially better than in earlier decades, with a current complication rate of ≈30% and a mortality rate of ≈3%. This improvement in

care can be credited to improvements in surgical and anaesthetic techniques, with better perioperative management, including nutritional support. Morbidity is a common cause for prolonged LOS and resource consumption by hospitals. For radical cystectomy the median LOS is highly variable, at 8–14 days in most recent series.

One approach to evaluating quality is the National Surgical Quality Improvement Program (NSQIP), which started in 1991 at 124 Veterans Administration (VA) Hospitals in the USA. This programme includes prospective data collection by well-trained nurse reviewers, who use standardized definitions of the variables to be collected. There is also rigorous inter-rater reliability and a validated risk-adjustment model. In addition, there are standardized endpoints established within the 30-day morbidity and mortality evaluation. This programme now has data on more than one million cases. More recently, there has been an expansion of this method into non-VA academic medical centres. The academic pilot project focused on three institutions (University of Kentucky, University of Michigan, and Emory University) and has now been expanded into 14 academic centres. The method has been validated and found to be as reliable in the academic setting as it was in the VA system. In general, the observed/ expected outcomes are similar between the VA and non-VA hospitals, after case-mix adjustment. The latter is an extremely important component of such prospective studies. Unfortunately, many earlier assessments by payer groups looked only at raw data without considering risk adjustment. This frequently gave a flawed evaluation of the quality of care provided. For example, the NSQIP data for surgery is evaluated by the observed/expected ratio of events to allow

comparisons among hospitals. The hospitals were initially ranked by unadjusted mortality rate. When the rank was altered by risk adjustment, the mortality rate commonly changed and several of the hospitals that were perceived as the best had a much less favourable rating after risk adjustment. Conversely, some hospitals that appeared not to do well improved substantially after risk adjustment, showing that they probably operated on patients with more complex problems.

To apply this method to a urology dataset our group examined 2538 radical cystectomies performed between 1991 and 2000. The cases were identified by CPT code, and the dataset included >100 clinical, operative and outcome variables. The study examined several outcomes. The 30-day mortality rate was 2.9%, comparable with most other retrospective and single-institution series. Notably the 90-day mortality rate was 6.8%, higher than commonly appreciated. A greater LOS or complication rate was associated with: (i) dependent functional status; (ii) elevated creatinine*; (iii) lower albumin*; (iv) longer operative duration*; (v) perioperative blood transfusion requirements*; (vi) age; (vii) ASA status; (viii) smoking history*; and/or (ix) surgeon experience*. The asterisk refers to circumstances that are potentially modifiable by improvements in structure or process. For example, it may be possible to decrease LOS or complication rates by improving renal function by relieving obstruction, improving preoperative nutritional status, or by ensuring optimal pulmonary function by having the patients stop smoking before surgery. Longer operative time, perioperative blood transfusion requirements, and surgeon experience are all interrelated to the volume of procedures done by the surgical team. The relationship between a higher volume of cases and better outcome in other complex surgical procedures such as esophagectomy or the Whipple procedure emphasizes concern that the surgeon who only does an occasional large case may have a higher complication rate.

The most important aspect of both the earlier NSQIP studies and our evaluation of cystectomy will be to more closely examine the data. The NSQIP annual report allows an examination of the observed/expected mortality ratios for all operations by hospitals. It is clear that some hospitals performed statistically better than the norm, while others were worse. Rather than a reward or punitive action, investigations focused on how to understand what activities took place in the hospitals that performed well, compared with those that were worse. This may allow a transfer of practices and procedures to the hospitals that did not perform as well, to ultimately improve their performance.

What does the speciality of urology do next to evaluate quality of care? First of all, in this era of healthcare cost containment, we need to focus on *value* as well as quality. Value is defined as quality/cost. No healthcare system is currently able to ignore cost issues. It is my opinion that our academic centres in urology are far behind other specialities. Unfortunately, the AUA does not have specific quality-of-care initiatives. However, an AUA Quality of Care and Patient Safety Committee has recently been formed to investigate these areas. In addition, there are several pilot programmes through governmental agencies or consortiums of payers and individual hospitals or groups of hospitals. We should all support these pilot programmes. We are probably much better off both as a speciality and as individuals to participate in the development of quality-of-care standards, rather than to react negatively once they are established. In urology we will also need a

cohort of well-trained urologists to lead these efforts in health services research and quality of care. There are established programmes through the Robert Wood Johnson Foundation and National Institutes of Health Training Grants, at centres such as University of California at Los Angeles and the University of Michigan, to train young individuals for careers as physician-scientists in the field of health services research.

The lead investigators in the NSQIP Cystectomy Project at the University of Michigan are Drs Brent Hollenbeck and John Wei. Other members of the investigative team at the University include: Drs Willie Underwood, David Miller, David Taub, Darrel Campbell, John Birkmeyer, and Rod Dunn. Individuals at the NSQIP Central Office include: Shukri Khuri, Jennifer Daley, and William Henderson.

REFERENCES

1 **Steinberg EP.** Improving the quality of care- can we practice what we preach? *N Engl J Med* 2003; **348**: 2681–3
2 **Birkmeyer JD, Dimick JB, Birkmeyer NJ.** Measuring the quality of surgical care: structure, process, or outcomes? *J Am Coll Surg* 2004; **198**: 626–32

THE PLACE OF THE AUGMENTED RECTAL POUCH IN URINARY DIVERSION

CHRISTOPHER R.J. WOODHOUSE – The Institute of Urology, University College London, and The Royal Marsden Hospital, London, UK

The human bladder has a great many failings; however, it remains the best means that we have of storing and evacuating urine. All the substitutes are much worse. Urologists should always attempt to conserve the natural lower urinary tract.

When a replacement is needed it is useful to think of three separate components; a reservoir, a sphincter mechanism and a conduit to the exterior. There are many published reports of complete replacement systems but there are great differences among patients, and many have requirements that make an 'off the shelf' reconstruction inappropriate. The reconstructive surgeon

must be the master of all of the components of lower tract replacement and select a system that is suitable for each individual.

The use of the rectum as a reservoir, the anal sphincters as a control mechanism, and the anus as a conduit, has a long and mainly dishonourable history. The much cited original description of the ureterosigmoidostomy by Simon in 1852 [1] was a report of the postmortem on his one patient. The literature of the first quarter of the last century records the legion of complications and deaths that accompanied this operation. It is ironic that just as the pathophysiology was becoming understood, the ileal conduit arrived and

dominated the diversion 'market' for 25 years.

So why is diversion into the rectum having its renaissance? There are two main reasons. The first is that Hohenfellner and Ghoneim, independently, recognized that which should have been obvious to all, i.e. that the pressure in the rectum had to be reduced. The second is that it has become apparent that all of the other lower tract replacements also have high complication rates.

Within all of the named systems of diversion and reconstruction, there are four broad categories; the conduit dripping into an external appliance, the orthotopic neobladder, the suprapubic continent catheterizable diversion, and the rectal pouch.

Published reports extol the virtues of the authors' favourite methods but give little guidance on the relative merits of each. There is a high degree of bias and lack of valid comparative data. The place of the rectal pouch can therefore only be decided on the basis of the perceived advantages and complications.

The present author's preferred variation on the rectal pouch is the Mainz II [2]. In this operation, 10 cm of rectum and 10 cm of lower sigmoid are detubularized and sutured together to form a pouch. In this respect it is similar to the other reservoirs made from large bowel. The ureters are then tunnelled into the bowel wall in a traditional manner. The slurry of urine and stool is passed through the anus.

It has the virtue of simplicity, especially after a radical cystectomy; the ureters and the rectum are just next to each other and waiting to be joined together. No re-packing of the intestines is needed and there is no intestinal anastomosis. It takes the same time to perform as an ileal conduit and is nearly an hour quicker than a continent suprapubic diversion.

The consequences and complications are, of course, legion. On the positive side, the patient evacuates in a reasonably natural manner at intervals similar to normal bladder emptying. Although the slurry is clearly different from stool, the patient does not have to learn a new technique. Clean intermittent self-catheterization is never needed. There are no appliances. The commonest metabolic complication, hyperchloraemic acidosis (HCA) is easy to detect and cheap to treat. Infective complications are rare. There is a very small risk of upper tract infection or stones. There are no reports of pouch stones or rupture.

On the negative side, the slurry does have an offensive, ammoniacal smell. It is not a very practical diversion for a patient living in a small, crowded apartment with only one lavatory. The risk of incontinence is 0–8%.

The incidence of HCA is uncertain. The risk seems to be cumulative with time and the follow-up of such patients is relatively short. If there is an analogy with the conventional ureterosigmoidostomy, it will be 50% at 10 years. It should not be used in patients who have had pelvic radiotherapy.

The most worrisome complication is anastomotic neoplasm. This tumour occurs at the reservoir/ureteric junction. It is thought to be a result of the mixture of urine and stool in contact with such an anastomosis. There are no reports of this condition in the Mainz II to date. However, in the conventional ureterosigmoidostomy, the incidence is 22% at 20 years of follow-up [3]. The tumours are adenomatous. Initially they are benign and appear to become malignant in a mean of 5 years. The earliest reported tumour is at 12 years from the formation of the ureterosigmoidostomy, and surveillance by flexible sigmoidoscopy is essential from about 10 years onwards. In patients having a cystectomy for cancer, this complication may not be relevant, but in young patients it is of critical importance.

Should the Mainz II prove unacceptable to the patient for any reason, the surgery to get rid of it is formidable. It is difficult to re-tubularize the pouch back into a rectum and sigmoid. It is possible to convert the pouch part into a reservoir for self-catheterization and anastomose the upper sigmoid to the lower rectum to restore bowel function. Obviously the pouch can be resected altogether. A covering colostomy may be needed. I do not know whether the pouch can just be abandoned and used as a capacious rectum for stool, with the urine diverted into a conduit; the low intrinsic pressure would probably lead to intractable constipation.

Apart from the surgical issues, the patients will be particularly interested in the quality of life. Here there are no reports; many authors state that the outcome of the operation is acceptable. It is seldom said to whom it was acceptable or by what criteria. We are left with the impression that it is acceptable to the surgeon.

Very few patients have experienced two successful bladder replacements. If a patient has an unsatisfactory diversion, another type may have a better outcome but does not provide a valid comparison. In my practice there is a small group of patients who had a successful conventional ureterosigmoidostomy in childhood 30 or more years ago. They are, apparently, happy with their lot. In 13 there has been an anastomotic neoplasm. None of these patients has volunteered to have an alternative diversion. All have wished to have the tumour resected and a new ureterosigmoidostomy formed. In two patients in whom this was not possible, a catheterizable pouch was made and both have expressed their dissatisfaction. It would seem that even having experienced the most serious complication, the patients preferred the ureterosigmoidostomy to any alternative.

The other replacements of the lower urinary tract also have their advantages and disadvantages. The incidence and importance is variable among the reports of different authors. It is not possible to say whether those of the Mainz II are better or worse. For each patient, the best that can be offered is a realistic appraisal of the options and allow a personal decision.

The augmented rectal pouch is an option for lower tract replacement that is just as valid as any other. It has a pattern of advantages and disadvantages that is no worse than any other. To me it seems preferable to an ileal conduit or a continent catheterizable diversion. It seems on a par with an orthotopic neobladder and under some circumstances may be preferable.

REFERENCES

1 **Simon J.** Ectopia vescicae (absence of the anterior walls of the bladder and pubic abdominal parietes): operation for directing the orifices of the ureters into the rectum; temporary success; subsequent death; autopsy. *Lancet* 1852; **2**: 568–70

2   **Fisch M, Wammack R, Muller SC, Hohenfellner R.** The Mainz pouch 2 (sigma-rectum pouch). *J Urol* 1993; **149**: 258–63

3   **Strachan JR, Woodhouse CRJ.** Malignancy following ureterosigmoidostomy in patients with exstrophy. *Br J Surg* 1991; **78**: 1216–8

BICALUTAMIDE 150 mg: PRACTICAL PRESCRIBING IN PATIENTS WITH EARLY PROSTATE CANCER

JOHN ANDERSON – Department of Urology, Royal Hallamshire Hospital, Sheffield, UK

The licensed indication for bicalutamide 150 mg has recently changed in the UK and several other countries. In the UK, bicalutamide 150 mg is indicated as an alternative to castration for patients with locally advanced prostate cancer, either alone or as an adjuvant therapy; it is no longer indicated in patients with localized disease who would normally be managed by observation. Whilst it would be unusual to commence hormone treatment in patients with clinically localized prostate cancer who would otherwise undergo watchful waiting, there nevertheless remains a degree of uncertainty within the clinical community about which patients should and should not be considered for bicalutamide 150 mg. This article reviews the conclusions of the most recent analysis of the bicalutamide Early Prostate Cancer (EPC) programme that have led to the changes in the license for prescribing bicalutamide 150 mg, and considers their clinical implications.

The ongoing EPC programme is the world's largest prostate cancer treatment study, involving >8000 patients [1]. Initiated in 1996, it consists of three complementary randomized, double-blind, placebo-controlled trials examining whether adding bicalutamide 150 mg/day to standard care (be it radical prostatectomy, radiotherapy or watchful waiting) can reduce the risk of prostate cancer progression and improve overall survival in patients with localized or locally advanced disease.

The latest analysis of the EPC programme data, in 2003 at a median of 5.4 years of follow-up [2], confirmed previous findings [3] that bicalutamide 150 mg significantly delays disease progression (hazard ratio, HR, 0.73; $P < 0.001$) [2] and prolongs the time to PSA failure (HR 0.49; $P < 0.001$) [4] compared with standard care alone. The greatest benefit was in patients at highest risk of progression. Given the relatively early stage of the study, it is hardly surprising that in the overall results there was no difference in survival between patients receiving placebo or bicalutamide 150 mg (HR 1.03; $P = 0.58$; 15% mortality) [2].

Further exploratory analyses, beyond the remit of the original protocol, revealed no difference in survival across all subgroups, except in those patients managed by observation. Within the watchful-waiting subgroup, with bicalutamide 150 mg there was a small trend toward reduced survival in patients with localized disease (HR 1.23; 95% CI 1.00–1.50) but a small trend toward prolonged survival in patients with locally advanced disease (HR 0.81; 95% CI 0.63–1.04) compared with observation alone [5]. The reduction in deaths in patients with locally advanced disease receiving bicalutamide was driven by a reduction in prostate cancer mortality. The increased deaths in patients with localized disease receiving bicalutamide was caused by a relative increase in deaths related to causes other than prostate cancer, which appear unrelated to any one specific cause [5].

So who should be considered for bicalutamide 150 mg therapy? The latest results from the EPC programme have shown that the greatest progression-free survival benefits for this treatment are in patients with locally advanced disease. As such patients are at significant risk of disease progression, any additional therapies that can reduce this risk, with minimal effects on lifestyle, are important.

The standard care for patients with locally advanced disease is often external-beam radiotherapy and, in this setting, the EPC programme data show that adding bicalutamide 150 mg as adjuvant therapy significantly reduces the risk of disease progression (HR 0.58; $P = 0.0035$) [6]. Furthermore, many patients with clinically localized disease who have had a radical prostatectomy are re-staged by the pathologist to pT3, or locally advanced disease, and here again adjuvant bicalutamide 150 mg significantly reduced the risk of disease progression (HR 0.71; $P = 0.0034$) [7]. Patients with locally advanced disease are not always suitable for, or opt not to receive, local therapy; under these circumstances, bicalutamide 150 mg again showed a significant risk reduction in terms of disease progression compared with observation alone (HR 0.53, $P < 0.001$) [5]. Moreover, as bicalutamide 150 mg has important quality-of-life advantages over castration, in terms of maintaining libido, allowing better physical activity and preserving normal bone mineral density [8,9], it offers an attractive alternative to androgen deprivation by surgical or medical castration.

In summary, the EPC programme continues to show, at a median of 5.4 years of follow-up, that bicalutamide 150 mg provides an important clinical benefit for patients with prostate cancer by reducing the risk of disease progression for those with locally advanced disease. It will be important to see whether these clinical benefits are maintained over time and ultimately translate into a survival advantage.

REFERENCES

1   **See WA, McLeod D, Iversen P, Wirth M.** The bicalutamide Early Prostate Cancer program: demography. *Urol Oncol* 2001; **6**: 43–7

2   **See W, Iversen P, McLeod D, Wirth M, Morris T, Carroll K.** Bicalutamide 150 mg alone or as adjuvant to standard care significantly improves progression-free survival in patients with early, non-metastatic prostate cancer (median 5.4 years' follow-up). *J Urol* 2004; **171** (Suppl): 214, A810

3   **See WA, Wirth MP, McLeod DG** *et al.* Bicalutamide as immediate therapy either alone or as adjuvant to standard care of patients with localized or locally advanced prostate cancer: first analysis of the Early Prostate Cancer program. *J Urol* 2002; **168**: 429–35

4   **See WA, Iversen P, McLeod DG** *et al.*

Bicalutamide 150 mg in addition to standard care significantly improves prostate-specific antigen progression-free survival in patients with early, non-metastatic prostate cancer: median 5.4 years' follow-up. *J Urol* 2004; **171** (Suppl): 280–1, A1062

5　Iversen P, McLeod D, See W *et al.* Bicalutamide ('Casodex') 150 mg in addition to watchful waiting in patients with early non-metastatic prostate cancer: updated analysis at a median 5.4 years' follow-up. *Eur Urol* (Suppl) 2004; **3**: 47, A180

6　McLeod D, Iversen P, See W *et al.* Bicalutamide ('Casodex') 150 mg as adjuvant to radiotherapy significantly improves progression-free survival in early non-metastatic prostate cancer: results from the bicalutamide early prostate cancer programme after a median 5.4 years' follow-up. *Eur Urol* (Suppl) 2004; **3**: 48, A182

7　Wirth M, Iversen P, McLeod D *et al.* On behalf of the 'Casodex' Early Prostate Cancer Trialists' Group. Bicalutamide ('Casodex') 150 mg as adjuvant to radical prostatectomy significantly increases progression-free survival in patients with early non-metastatic prostate cancer: analysis at a median follow-up of 5.4 years. *Eur Urol* (Suppl) 2004; **3**: 48, A181

8　Anderson J. Treatment of prostate cancer – The role of primary hormonal therapy. *EAU Update Series* 2003; **1**: 32–9

9　Anderson J. The role of antiandrogen monotherapy in the treatment of prostate cancer. *BJU Int* 2003; **91**: 455–61

SUPPRESSOR SCREENING – A POTENTIAL NEW MODEL FOR UNDERSTANDING THE GENETIC COMPONENTS OF UROLOGICAL MALIGNANCIES   SASHI KOMMU – St Anthony's Hospital, Surrey, UK

For centuries our energies have been channelled into finding the causes of disease processes; the reason for this is obviously to satisfy the quest for knowledge and to link cure or treatment of disease process to the cause. The concept of suppressor screening is a novel approach in genetics, which aims to identify directly the genes which provide a cure to a certain condition rather than identifying the genes which cause the condition.

A typical scientific model for studying a disease process involves three main steps. First, the aim is to find an animal (e.g. a strain of mouse or rabbit) that develops the disease process, or to find a way of triggering the disease process in the same animal. This is followed by a study of the mechanism and understanding of the disease as it develops. Finally, a drug is designed to treat the condition. This is a simplistic model but many studies fit this basic pattern. However, the causative mechanism can be bypassed and the result created in a group of genetically manufactured organisms in which the disease process tends to be reproduced. These organisms can then be studied to see which genes protect against the development of the disease process.

An example of this is the study by Carpinelli *et al.* [1], in which genetic screens in mice, particularly those that identify modifiers of pre-existing genetic defects, have been used successfully to order components of complex signalling pathways. An agent that causes random mutations was injected into hundreds of mice with a genetic defect that causes thrombocytopaenia. Thousands of direct offspring were then screened to reveal seven healthy mice. These were then studied to reveal one of three different potential mutations, which could cure the disease. In theory, targeted drugs for the protein coded for by the normal gene could potentially cure thrombocytopaenia.

This model could be exploited in urological diseases. The PAC120 xenograft is a relatively new model of hormone-dependent prostate cancer, providing an opportunity to study the hormone-dependence escape mechanism and to evaluate the efficacy of new therapeutics

[2]. This model of suppressor screening can be used in xenografted mice to decipher which genes protect against hormone escape in prostate cancer, or indeed the development of the disease itself.

The Eker rat model of hereditary renal carcinoma is an example of a Mendelian dominantly inherited predisposition to a specific cancer in an experimental animal. Forty years after the discovery of the Eker rat in Oslo, Hino *et al.* [3] and Knudson's group [4] independently identified a germline retrotransposon insertion in the rat homologue of the human tuberous sclerosis (TSC2) gene. This was perhaps the first isolation of a Mendelian dominantly predisposing cancer gene in a naturally occurring animal model. This rat was named the 'Nihon' rat and its predisposing (Nihon) gene could be a novel renal tumour-suppressor gene. A new hereditary renal carcinoma in the rat was subsequently found. Mass 'grooming' of such rats will produce renal cancer in each subsequent reproductive population. The model of suppressor screening can then be applied to look at the few rats that do not develop the malignancy, and these mice selectively tested for genes that may have rendered them immune to developing the malignancy. The extrapolation of this concept to humans may be in its infancy, but can be envisaged in the near future.

Currently there is good epidemiological evidence for prostate cancer susceptibility genes, but no major locus has been unequivocally identified. A genome-wide search was conducted from an international consortium (ACTANE) [5]. About 90% of the prostate cancers identified in this study were clinically detected. Eight loci with preliminary linkage evidence (heterogeneity LOD > 1.0) have been identified. Genetic susceptibility to prostate cancer is likely to be controlled by many loci, with no single gene explaining a large fraction of the familial risk. One way of identifying prostate cancer susceptibility genes is to extrapolate the concept of suppressor screening to the human model or using xenografted PAC120 mice.

An example of the extrapolated applicability of this approach in understanding urological disease is illustrated by Legrier *et al.* [6], where there were mucinous differentiation features associated with hormonal escape in a human prostate cancer xenograft. Using PAC120

and its hormone-independent variants, the expression of mucins (e.g. MUC1 and MUC2) were analysed by immunohistochemistry or RT-PCR. The resulting data indicated mucinous differentiation as an important step in acquiring hormone independence in this cancer, and suggested that secretory mucins might participate in an unknown pathway of hormonal escape in prostate cancer.

The technique of suppressor screening has been described previously and used to study the biological function of fruit flies and worms. It has not been exploited in vertebrates and its potential for finding cures is one that should be explored further in urological malignancies. This model has the potential to accelerate the understanding of disease processes. Approaches such as the one described not only help in understanding disease processes but also may potentially do so at an exponential rate. It has specific advantages in researching conditions such as prostate cancer in which disease progression is often slow yet the consequences potentially devastating.

REFERENCES

1 **Carpinelli MR, Hilton DJ, Metcalf D et al.** Suppressor screen in Mpl–/– mice. c-Myb mutation causes supraphysiological production of platelets in the absence of thrombopoietin signaling. *Proc Natl Acad Sci USA* 2004; **101**: 6553–8

2 **Legrier ME, de Pinieux G, Poirson-Bichat F et al.** A new model of human prostate cancer, the PAC120 xenograft. *Pathol Biol (Paris)* 2003; **51**: 1–4

3 **Hino O, Kobayashi T, Momose S, Kikuchi Y, Adachi H, Okimoto K.** Renal carcinogenesis. genotype, phenotype and dramatype. *Cancer Sci* 2003; **94**: 142–7

4 **Yeung RS, Xiao GH, Jin F, Lee WC, Testa JR, Knudson AG.** Predisposition to renal carcinoma in the Eker rat is determined by germ-line mutation of the tuberous sclerosis 2 (TSC2) gene. *Proc Natl Acad Sci USA* 1994; **91**: 11413–6

5 **Edwards S, Meitz J, Eeles R et al.** Results of a genome-wide linkage analysis in prostate cancer families ascertained through the ACTANE consortium. *Prostate* 2003; **57**: 270–9

6 **Legrier ME, de Pinieux G, Boye K et al.** Mucinous differentiation features associated with hormonal escape in a human prostate cancer xenograft. *Br J Cancer* 2004; **90**: 720–7

Correspondence: sashi.kommu@ icr.ac.uk