dose of loratadine ($n=7$), three times that dose ($n=22$), or a corn-oil control ($n=13$).

Gross and histological assessment of male fetuses revealed that 28% in the low-dose group and 35% in the high-dose group exhibited hypospadias ($P=0.0001$), confirmed by 3D reconstruction analysis. None of the male controls displayed developmental abnormalities.

Quantitative REVERSE TRANSCRIPTION-POLYMERASE CHAIN REACTION (RT-PCR) analysis showed that males (with and without hypospadias) and females exposed to loratadine showed a significant increase in androgen receptor mRNA expression compared with same-sex controls ($P=0.01$). Males, but not females, exposed to loratadine showed a significant increase in estrogen receptor mRNA expression compared with male controls ($P=0.02$), but no difference was seen between loratadine-exposed males without hypospadias and controls.

From these results, the authors suggest that loratadine exerts endocrine-disrupting effects in the developing mouse fetus by acting as an antiandrogen or as an estrogen mimic.

Tamsin Osborne

Original article Willingham E *et al.* (2006) Loratadine exerts estrogen-like effects and disrupts penile development in the mouse. *J Urol* 175: 723–726

Neuro-fuzzy modeling accurately predicts bladder-cancer progression

Transitional-cell carcinoma (TCC) is the most common form of bladder cancer, and most TCC-related deaths occur after it progresses. To date, the use of molecular biomarkers to predict future tumor behavior has been disappointing, so Catto *et al.* compared the use of ARTIFICIAL NEURAL NETWORKS (ANN) and NEURO-FUZZY MODELING (NFM) with logistic regression in predicting tumor progression.

From a single center, the authors randomly selected 117 patients with primary TCC. Of these, 107 had bladder tumors, mostly males with a history of smoking. Patients underwent tumor excision, chemotherapy, and BACILLUS CALMETTE-GUÉRIN immunotherapy. The team collected clinicopathologic data including tumor stage and grade, patient age, sex and smoking history, as well as measuring methylation at 11 loci and P53 expression—markers that seem more specific for invasive, rather than

superficial, TCC. For all models, these data were used in five separate combinations.

NFM was superior to both other models when predicting tumor progression, showing 88–100% sensitivity, 97–100% specificity and 94–100% accuracy, depending on the data combination used. When NFM was used with all data it produced 100% sensitivity, specificity and accuracy. NFM was also more accurate in predicting the timing of tumor progression from clinicopathologic data, having an average error of 5 months, compared with 9 months for ANN ($P=0.002$), and >1 year for linear regression ($P=0.00005$).

NFM is an accurate, easy-to-interpret method for predicting tumor progression that, unlike ANN, can be translated into graphic outputs.

Chrissie Giles

Original article Catto JWF *et al.* (2006) Neuro-fuzzy modeling: an accurate and interpretable method for predicting bladder cancer progression. *J Urol* 175: 474–479

Predicting male hypogonadism using an artificial neural network

HYPOGONADISM is a common disorder in aging men that can lead to significant health problems. This condition can be treated with testosterone replacement therapy, but because the clinical presentation can be varied, identifying hypogonadism is challenging.

Kshirsagar *et al.* used four different analytical methods—logistic regression, linear and quadratic discriminant function analysis and an artificial neural network (ANN)—to predict hypogonadism (serum testosterone level <300 ng/dl based on easily ascertained variables. Age, erectile dysfunction (ED), depression and serum testosterone level were evaluated in 218 men. ED and depression were assessed using validated questionnaires (the Sexual Health Inventory for Men and the Center for Epidemiologic Studies Depression Scale, respectively). The men were randomly allocated to a training set ($n=148$) or a test set ($n=70$).

The ANN was able to accurately predict hypogonadism, with a one hidden layer, four hidden node network proving the most accurate. The receiver-operating characteristic curve was 0.725. All three variables were necessary for accurate classification, and the

GLOSSARY

REVERSE TRANSCRIPTION-POLYMERASE CHAIN REACTION (RT-PCR)

A variation of the PCR technique in which cDNA is made from RNA via reverse transcription and the cDNA is then amplified using standard PCR protocols

ARTIFICIAL NEURAL NETWORKS

A complex computer program that simulates the physiologic processing of a neural pathway

NEURO-FUZZY MODELING

An artificial neural network which uses fuzzy logic, and so is open to interrogation by the user

BACILLUS CALMETTE-GUÉRIN

A live attenuated strain of *Mycobacterium tuberculosis* that stimulates an immune response against cancer cells within the bladder

P53

A protein that suppresses abnormal cell proliferation; abnormalities in p53 are frequently detected in human tumors

HYPOGONADISM

Abnormally decreased functional activity of the gonads leading to decreased production of gonadal hormones