Cellular Oncology 27 (2005) 355
IOS Press

Letter to the Editor

Ki67 predicts progression in early CIN: Validation of a multivariate progression-risk model

To the Editor,

A recent work by Kruse et al. [1], carried out to verify whether CIN 3 lesions are a "matter of co-existence or true progression", demonstrated a higher prognostic accuracy of Ki67 quantitation over the histopathological classification of uterine cervix intraepithelial neoplasia. The authors specify that the prognostic value consists in the prediction of progression of CIN 1 and 2 lesions to CIN 3. Prognostic marker evaluations are carried out with an automated interactive image analysis system, which permits the quantitation of "Ki67 features".

Two different types of Ki67 evaluations, the 90th percentile of the stratification index and the percentage of Ki67 positive cells in the middle third layer of the epithelium were combined together in a progression risk model that permits the classification of patients with CIN 1 and 2 lesions into two subgroups at high and low risk. This method appears somewhat complicated and at the very least requires rigorous quality controls on determination intra-reproducibility because of the immunoperoxidase staining used and possible background biases. Moreover, I wonder how diffuse the analysis system is in Pathology Units.

Having said that, it must be recognised that the negative predictive value of the model was 100%, that is, none of the CIN 1 or 2 "Ki67 model low-risk" cases progressed to CIN 3 during a mean follow-up of 3.4 years. However, as stated by the Authors themselves, the progression rates from CIN 1/CIN 2 to higher grade lesions are fairly low and it would therefore be important to identify lesions that will definitely progress rather than those that will not. Unfortunately, the positive predictive value for Ki67 model is only 30%, that is less than one third of low-grade "Ki67 model high-risk" lesions which actually progressed to higher grade lesions. Doesn't this mean that 70% of low-grade "Ki67 model high-risk" lesions are actually "over-diagnosed" by the proposed prognostic model?

If the Authors' goal was to predict low-grade CIN progression, I wonder how, with such a low predictive capacity, Ki67 quantitation could possibly modify the current clinical follow-up of these patients.

Reference

[1] A.J. Kruse, J.P.A. Baak, E.A. Janssen, K.H. Kjellevold, B. Fiane, K. Lovslett, J. Bergh and S. Robboy, Ki67 predicts progression in early CIN: Validation of a multivariate progression-risk model, *Cell. Oncol.* **26** (2004), 13–20.

Rosella Silvestrini, PhD
Istituto Nazionale per lo Studio e la Cura dei Tumori,
Via Venezian 1, 20133 Milan, Italy
E-mail: silvestrini@istitutotumori.mi.it