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## MCM-2 is a better proliferation marker than KI-67 in renal cell carcinomas

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**Introduction/Background:** Fuhrman nuclear grade is the most important histological parameter to predict prognosis in a patient of renal cell carcinoma (RCC). However, it suffers inter-observer and intra-observer variation giving rise to need of a parameter that not only correlates with nuclear grade but is also objective and reproducible. Proliferation is the measure of aggressiveness of a tumour and it is strongly correlated with Fuhrman nuclear grade, clinical survival and recurrence in RCC. Ki-67 is conventionally used to assess proliferation. However, renal cell carcinoma has a low proliferating fraction due to which it is unsuitable for routine semi-quantitative analysis. Mini-chromosome maintenance 2 (MCM-2) is a lesser known marker of proliferation and identifies a greater proliferating fraction. This study was designed to assess the labelling index of MCM-2 as compared to Ki-67 by both quantitative and semi-quantitative analysis and to relate this expression with Fuhrman nuclear grade in RCC.

**Material and Methods:** A total of n=50 biopsies of various histological subtypes, grades and stages of RCC were selected from patients of adult age group. Immunohistochemical staining using Ki-67 (MIB-1, Mouse monoclonal antibody, Dako) and MCM-2 (Mouse monoclonal anti-body, Thermo) was performed on the paraffin embedded blocks and labelling indices (LI) were determined by two pathologists independently. Both quantitative and semi-quantitative analyses were performed. Statistical analysis was carried out using SPSS 20.0. Kruskal-Wallis test was used to determine a correlation of proliferation markers with grade and Pearson's correlate was used to determine correlation between both proliferation markers. Finally, Spearman's correlate was carried out to determine correlation between quantitative and semi-quantitative analysis for both markers.

**Results:** Labelling index of MCM-2 (median=24.29%) was found to be much higher than Ki-67 (median=13.05%). Both markers were significantly related with histological grades of RCC ( $p=0.00$ ; Kruskal-Wallis test). LI of MCM-2 was found to correlate significantly with LI of Ki-67 ( $r=0.0934$ ;  $p=0.01$  with Pearson's correlate). Semi-quantitative analysis of MCM-2 was found to be accurate even for cases with low proliferative potential (grade I= $0.884$ ;  $p=0.004$ , Spearman's correlate) as compared to Ki-67 (grade I= $-0.51$ ;  $p=0.904$ ) which showed no relationship with quantitative analysis in those cases.

**Conclusion:** Both Ki-67 and MCM-2 are markers of proliferation which are closely linked to the tumour histological grade. However, the low proliferation fraction identified by Ki-67 makes its analysis difficult outside a research lab. MCM-2 on the other hand can be used reliably to determine the proliferation fraction of the tumour in a semi-quantitative analysis and thus is an objective and reproducible parameter that can help complement Fuhrman nuclear grade to determine the aggressiveness of the tumour.

### Biography

Muhammad Zain Mehdi after completing his early education acquired MBBS degree from Punjab Medical College, Faisalabad Pakistan and was one of the position holders at the end of the term. He completed his foundation year in the Allied Hospital Faisalabad and joined University of Health Sciences Lahore Pakistan to pursue his Masters of Philosophy in Morbid Anatomy and Histopathology. Currently he is a resident for FRC Path II training at Shaukat Khanum Memorial Cancer Research Hospital Lahore, Pakistan

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