

**Clinical Genomics Laboratory**  
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**Website: <http://www.cml.md/genomics/>**  
 Patient: XXXXXXXXXXXXXXXX

**Patient Name:** XXXXXXXXXXXX  
**Gender:** X  
**Date of Birth:** XX/XX/XXXX  
**Specimen Type:** OCT-embedded  
**Submitters Name:** Dr. XXXXXXXXXXXX  
**Submitters Institution:** XXXXX

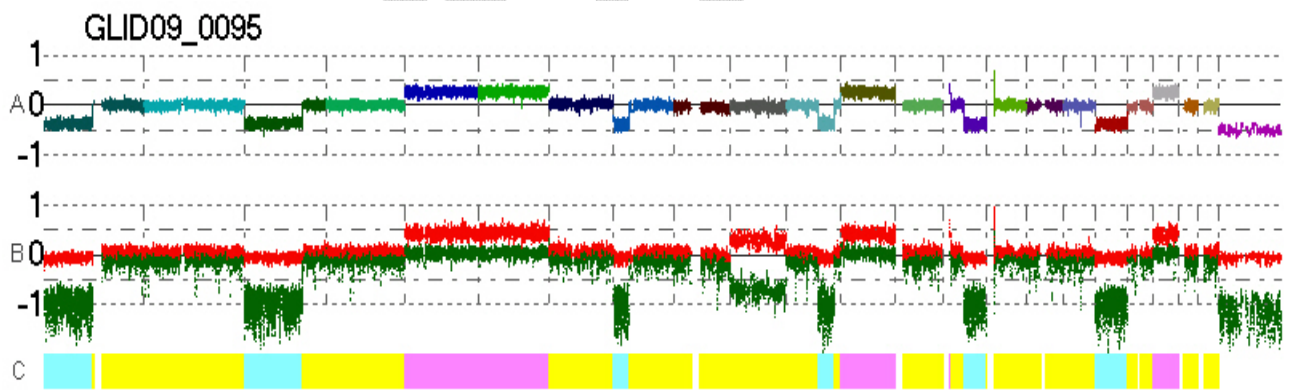
**CML Accession Number:** CML09-GDXXXXX  
**Date specimen obtained:** XX/XX/XXXX  
**Date specimen received:** XX/XX/XXXX  
**Report date:** XX/XX/XXXX  
**Test:** SNP array karyotype  
**Test Indication:** Renal mass, 4.5 cm

**Result:**

Tumor, right kidney, SNP oligonucleotide microarray karyotype (SP09-XXXX):  
 Loss of chromosomes 3p, loss of 14q, and additional cytogenetic abnormalities, see comment.

Comment: Loss of 3p supports the morphologic diagnosis of conventional clear cell renal carcinoma. Loss of 14q in renal clear cell carcinoma has been associated with adverse prognosis. Additional chromosomal changes are present in this tumor, but the clinical relevance of these additional changes, if any, is not known. They are listed in the table in the interpretive component of this report.

**Interpretation:** Nearly 100% of conventional clear cell renal carcinomas have loss of 3p.<sup>1</sup> They may also have additional cytogenetic abnormalities with prognostic significance, such as loss of 9p or 14q.<sup>2</sup> Loss of 9p is an independent predictor of poor survival in patients with conventional clear cell RCC and should be integrated into prognostic models.<sup>2,3</sup> It has been consistently reported that loss of chromosome 14q is associated with higher grade and stage<sup>4,6</sup>. Furthermore, these have been linked with adverse prognosis and diminished disease-specific survival.<sup>5</sup> However, loss of 14q was not an independent predictor of survival.<sup>3,5</sup>



CopyNumber Color Code		
Deletions	Normal/diploid	Gains
Dark blue = 0	Yellow = 2	Pink = 3
Light blue = 1		Pink-Red = 4
		Red = amplified

Whole genome view SNP array karyogram for this sample. Chromosomes are plotted in numeric order from left (chromosome 1) to right (X chromosome). A) Log2ratio, zero = copy number of 2. B) Allele-specific analysis of copy number. C) The copy number Hidden Markov Model (HMM) is color-coded as indicated to the left.

Copy Number	Chromosome	StartPos	EndPos	Length (Mb)	StartCytoband	EndCytoband
1	1	825852	119736169	118.910	p36.33	p12
1	3	48603	142238276	142.190	p26.3	q23
3	5	81949	180625439	180.543	p15.33	q35.3
3	6	119769	170791203	170.671	q25.3	q27
1	8	180568	36219874	36.039	p23.3	p12
2*	10	148946	135295604	135.147	p15.3	q26.3
1	11	79477795	117685151	38.207	q14.1	q23.3
3	12	50446	132377151	132.327	p13.33	q24.33
1	14	51160067	106355525	55.195	q22.1	q32.33
1	18	210071	76115293	75.905	p11.32	q23
3	20	17408	62374986	62.358	p13	q13.33
1	23	142664	154353200	154.211	p22.33	q28

**Genomic position and cytogenetic break points for CML09-GDXXXXX.** Asterisk indicates copy neutral loss of heterozygosity (acquired uniparental disomy).

### Summary of Cytogenetic Abnormalities in Renal Epithelial Tumors

Several renal tumors have characteristic cytogenetic abnormalities that can aid in the classification of morphologically challenging cases. The cytogenetic abnormalities can be identified by SNP array virtual karyotyping of fresh or formalin-fixed paraffin embedded tumor samples.<sup>7,8</sup> Nearly 100% of conventional clear cell renal carcinomas have loss of 3p.<sup>1</sup> They may also have additional cytogenetic abnormalities with prognostic significance, such as loss of 9p or 14q.<sup>2</sup> Papillary renal cell carcinomas classically show trisomies of chromosomes 7 and 17.<sup>9</sup> Chromophobe renal cell carcinomas are hypodiploid with losses of multiple chromosomes, most commonly chromosomes 1, 2, 6, 10, 13, 17 and 21.<sup>9</sup> Oncocytomas are benign renal epithelial tumors with no or few cytogenetic abnormalities. When cytogenetic abnormalities are present in oncocytomas, the most common is complete or partial loss of chromosome 1 (40% of cases), but monosomy 14 (15%), and trisomy 7 (5%) can also be seen.<sup>7</sup>

**Methods:** DNA was extracted from OCT-embedded tumor following pathologist review of the H&E stained slide. Whole genome comparative genomic hybridization was done using Affymetrix 250K *Nsp* SNP array which can detect uniparental disomy and copy number changes as small as 500kb when performed on fresh DNA. The resolution of paraffin embedded tumors will vary based on the quality of the DNA. The assay was performed according to the manufacturer's protocol. Analysis was performed using Affymetrix™ GTYPE 2.0.1, CNAGv3.0<sup>10</sup>, and oneClickCGH (InfoQuant LTD, London, UK) software programs. The normal reference DNA used for analysis was chosen by the CNAG software from a library of data files obtained from normal specimens. All controls performed as expected.

### References:

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4. Alimov A, Sundelin B, Wang N, Larsson C, Bergerheim U. Loss of 14q31-q32. 2 in renal cell carcinoma is associated with high malignancy grade and poor survival. *Int J Oncol.* 2004;25(1):179-185.
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10. Yamamoto G, Nannya Y, Kato M, et al. Highly sensitive method for genomewide detection of allelic composition in nonpaired, primary tumor specimens by use of affymetrix single-nucleotide-polymorphism genotyping microarrays. *Am J Hum Genet.* Jul 2007;81(1):114-126.

*This SNP based oligonucleotide microarray assay was developed by Affymetrix, Inc (Santa Clara, CA, USA) and its performance determined by the Genomics Laboratory of Creighton Medical Laboratories for the sole purpose of identifying the gain or loss of DNA copy numbers and regions of loss of heterozygosity. This microarray will not detect balanced chromosomal aberrations such as Robertsonian translocations, reciprocal translocations, inversion or balanced insertions, nor imbalances in regions that are not represented on the microarray, nor low-level mosaicism or tumor burden. The method is based on relative copy number estimates; therefore polyploidy cannot be reliably detected without a cell-based assay. Clinical implications of chromosomal aberrations may not be unknown at the time of analysis. This test is used for clinical purposes. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. Pursuant to the requirement of CLIA'88, this laboratory has established and verified the test's accuracy and precision.*