The c-Myc Target Gene Rcl (C6orf108) Encodes a Novel Enzyme, Deoxynucleoside 5′-monophosphate N-Glycosidase*

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RCL is a c-Myc target with tumorigenic potential. Genome annotation predicted that RCL belonged to the N-deoxyribosyltransferase family. However, its putative relationship to this class of enzymes did not lead to its precise biochemical function. The purified native or N-terminal His-tagged recombinant rat RCL protein expressed in Escherichia coli exhibits the same enzyme activity, deoxynucleoside 5′-monophosphate N-glycosidase, never before described. dGMP appears to be the best substrate. RCL opens a new route in the nucleotide catabolic pathways by cleaving the N-glycosidic bond of deoxynucleoside 5′-monophosphates to yield two reaction products, deoxyribose 5-phosphate and purine or pyrimidine base. Biochemical studies show marked differences in the terms of the structure and catalytic mechanism between RCL and of its closest enzyme family neighbor, N-deoxyribosyltransferase. The reaction products of this novel enzyme activity have been implicated in purine or pyrimidine salvage, glycolysis, and angiogenesis, and hence are all highly relevant for tumorigenesis.

The c-Myc transcription factor plays an important role in the regulation of the cell cycle, cellular transformation, and apoptosis (1) as well as in the genesis of many human cancers (2). The deregulation of MYC expression by chromosomal translocation, amplification, or altered signal transduction is commonly found in human cancers (3, 4). To elucidate the mechanisms by which c-Myc contributes to tumorigenesis, several approaches have been used to identify its target genes, which are compiled in the database myccancergene.org.

Rcl was identified as a c-Myc target by representational difference analysis between non-adherent Rat1a fibroblasts and Rat 1a cells transformed by MYC (5). Rcl is expressed at a low level in untransformed cell lines, although it is significantly elevated in breast cancer and lymphoma cell lines (5). Moreover, Rcl is one of the most responsive targets to Myc activation in vitro and in Myc-induced transgenic lymphoma (6, 7), and Rcl has been shown to be a direct Myc target in a human lymphoma cell model (8). Serial analysis of gene expression studies revealed that Rcl is also highly expressed in human glioblastoma multiforme as compared with normal human brain (information from the UniGene data base, at NCBI). Furthermore, Rcl is among the top 50 genes whose overexpression distinguishes between benign and malignant prostate tissues (9). Functionally, Rcl has transforming activity in Rat1a cells when coexpressed with either vascular endothelial growth factor or lactate dehydrogenase (10). Altogether, these data suggest that RCL could be a prime therapeutic target.

RCL appears to be a nuclear 22-kDa protein with yet unknown function. The closest relatives of RCL protein are members of the nucleoside 2-deoxyribosyltransferase family (EC 2.4.2.6). (pfam 05014), which catalyze the reversible transfer of the deoxyribosyl moiety from a deoxynucleoside donor to an acceptor nucleobase (11–13). Here, we report the purification and characterization of the recombinant RCL from rat. RCL is a deoxynucleoside 5′-monophosphate N-glycosidase, an enzyme never described before. Its putative role in the mammalian nucleotide metabolism and tumorigenesis is also discussed.

EXPERIMENTAL PROCEDURES

Chemicals—Ribonucleosides and deoxyribonucleosides, mono-, di-, and triphosphate derivatives of adenine, cytosine, guanine, hypoxanthine, thymine, and uracil were from Sigma-Aldrich. 6-Methylthio- guanosine 5′-monophosphate, 2′,3′-deoxy- yguanosine 3′-monophosphate, and 8-oxo-deoxyguanosine 5′-monophosphate were from Jena Bioscience.

Overexpression and Purification of RCL and of the N-terminal His-tagged RCL—The Rcl cDNA cloned into pCR2.1 as a Ncol-BamHI fragment was subcloned into pET24d digested with the same restriction enzymes. The resulting pET24dRcl was used to transform strain BL5 (BL21 (DE3) pDIA17). One liter of LB medium supplemented with 50 μg/ml of chloramphenicol and kanamycin was inoculated with an overnight culture of BL5 containing pET24dRcl. The culture was grown under agitation at 37 °C until an A600 of 0.8. Isopropyl-1-thio-β-D-galactopyranoside was added to a final concentration of 1 mM and the cultures further incubated for 3 h. Bacteria were harvested by centrifugation at 4500 × g for 20 min at 4 °C and the pellet frozen at −20 °C. The cells were resuspended in 35 ml of 50 mM Tris, pH 7.5, and broken by two passages through a French press at 14,000 pounds/square inch. The lysate was cen-
trifuged at 25,000 × g for 30 min at 4 °C. The supernatant was loaded on a Q-fast flow column previously equilibrated with the same salt buffer. Proteins were eluted with a 0–40% NaCl gradient. RCL was eluted between 20 and 25% NaCl, and the corresponding fractions were pooled and precipitated with solid ammonium sulfate. Pelleted RCL was resuspended in Tris 50 mM, pH 7.5, and further purified by filtration on a Sephacryl S-200 column previously equilibrated with the same buffer. The elution was followed by UV absorption at 280 nm, and each fraction was analyzed by SDS-PAGE electrophoresis and N-glycosidase activity. The purest and most active fractions were concentrated on an Omega cell with a 10,000 molecular weight cutoff membrane (Pall Life Sciences) and stored at −20 °C.

The N-terminal His-tagged RCL was overproduced and purified as follows. The Rel gene cloned into pCR2.1 as a Ndel-BamHI fragment was subcloned into pET28a digested with the same restriction enzymes. The resulting plasmid, pET28aRcl, was transformed into strain BL21. Culture conditions and induction were performed as described above. Frozen cells resuspended in 40 ml of extraction/wash buffer (50 mM NaH2PO4, Na2HPO4, 300 mM NaCl pH 7.0) were broken by two passages through a French press at 14,000 pounds/square inch. The lysate was centrifuged at 25,000 × g for 30 min at 4 °C. The supernatant was loaded on a column containing 6 ml of TALON resin (BD Biosciences) previously equilibrated with the same buffer. After washing, RCL was eluted with 150 mM imidazole. Fractions containing RCL were pooled and concentrated on an Omega cell 10 K membrane (Pall). The His-tagged RCL was further purified by gel filtration on a Sephacryl S-200 column. The purity was checked by SDS-PAGE electrophoresis and by measuring the specific activity. Purified His-tagged RCL was stored at −20 °C.

RCL with Glu-105 Replaced by Ala (E105A Mutant) by Site-directed Mutagenesis—Oligonucleotides T7prom (5'-GGCGGAAATTTAATAGCAGCTACTATAGGGG-3') and olinvE105A (5'-GCCGCCGCCAGCCGATAGCAGCAACACCCAG-3'), T7term (5'-GGGGTTATGCTAGTTATTGCTACGCGG-3') and olE105A (5'-CTTGGGTGTTGGCTATGCGCTGGGC-CGCCG-GGCC-3') were used in two separate PCRs with plasmid pET28aRcl as the DNA template. The parameters used were 1 cycle of 5 min at 95 °C, 25 cycles of 30 s at 95 °C, 30 s at 51.5 °C, and 1 min at 72 °C, and 1 cycle of 10 min at 72 °C. An aliquot (1/100 of the reaction) of each PCR was used as the DNA template in a third PCR with oligonucleotides T7prom and T7term. The parameters used were the same as described above. The PCR product was purified by using the QIAquick PCR purification kit (Qiagen) and then digested with Ndel and BamHI enzymes over 2 h at 37 °C and repurified. Each PCR product was ligated with plasmid pET28a digested with the same restriction enzymes. The ligation mixtures were used to transform strain DH5α. Plasmids with the correct sequence, pET28aRclE105A, were used to transform strain BL21.

Enzyme Activity Assays—The enzyme activity was determined either spectrophotometrically by following one of the reaction products, hypoxanthine or deoxyribose 5-phosphate, or by HPLC3 separation and UV detection of the released nucleobase and the remaining substrate.

dIMP was used as a substrate, and the hypoxanthine released oxidized to uric acid by xanthine oxidase. The absorption increase at 290 nm was converted in enzymatic units using a millimolar absorbance coefficient of 12.0. One milliliter of the medium reaction thermostated at 37 °C contained 50 mM Tris-HCl, pH 7.5, 1 mM dIMP, 0.2 units of xanthine oxidase (Roche Applied Sciences) and 50–200 μg of purified RCL.

d-Glyceraldehyde-3-phosphate, which is produced by the deoxyribose 5-phosphate aldolase from deoxyribose 5-phosphate, was coupled to the oxidation of NADH to NAD via the reactions catalyzed by triose phosphate isomerase and glycerol 3-phosphate dehydrogenase. The decrease in absorbance at 340 nm was followed on an Amersham Biosciences Ultrospect 3100 Pro spectrophotometer using a millimolar absorbance coefficient of 6.22. The reaction medium (1 ml final volume) contained 50 mM Tris acetate, pH 6.0, 0.1 mM NADH, and 1.5 units each of glycerol-3-phosphate dehydrogenase, triose phosphate isomerase (Roche Applied Sciences), deoxyribose-5-phosphate aldolase,4 and 50–200 μg of purified RCL. One unit of enzyme activity corresponds to 1 μmol of product formed in 1 min at 37 °C and pH 6.0.

HPLC assays were as described previously (14). Hydrolase activities (dNMP → N + dR5P) were performed at 37 °C in 50 mM Tris acetate, pH 6.0, containing 1 mM dNMP and the appropriate amount of purified RCL. The reverse reaction (Gua + dR5P → dGMP) was performed at 37 °C in 50 mM Tris acetate, pH 6.0, containing 3 mM guanine, 3 mM deoxyribose 5-phosphate, and 200 μg of purified RCL. Deoxyribose 5-phosphate transferase reactions (dNMP + X → dXMP + N) were performed at 37 °C in Tris acetate, pH 6.0 (or 50 mM Tris-HCl, pH 7.5, or 50 mM citrate-sodium, pH 6.5), containing 1 mM dCMP or dGMP and 1 mM either adenine, cytosine, guanine, thymine, uracil, or hypoxanthine and 200 μg of purified RCL.

The Ndel-HindIII fragment of phSP234, which contains the Escherichia coli deoC gene (a kind gift of H. Sakamoto) was cloned into plasmid pET28a digested with the same restriction enzymes. The resulting plasmid, in strain BL21, allows the expression of the deoxyribose 5-phosphate aldolase with an N-terminal His tag. Culture condition, induction, centrifugation, and purification on TALON resin were as described for His-RCL. Fractions containing deoxyribose 5-phosphate aldolase were dialyzed extensively against 10 mM Tris, pH 7.5, 50 mM NaCl, and 1 mM dithiothreitol concentrated in an Omega cell 10 K and kept frozen at −20 °C.

Other Analytical Procedures—Protein concentration was determined using the Bradford assay kit from Bio-Rad. SDS-PAGE was performed as described by Laemmli (15). Mass spectrometry was performed by the PT3 proteomique of the Pasteur Institute as previously described (14). Equilibrium sedimentation experiments were performed at 20 °C using a Beckman Optima XL-A analytical ultracentrifuge equipped with an An-60 Ti four-hole rotor. Samples (150 μl) at three protein concentrations (3, 10, and 30 μM), in 20 mM Tris-HCl, pH 7.5,

The abbreviations used are: HPLC, high pressure liquid chromatography; COG, clustering of orthologous groups.

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150 mM NaCl were run at six speeds (8, 10, 12, 14, 20, and 50 kilorotations/min). Five profiles were recorded after reaching equilibrium (12–18 h) at three wavelengths according to sample concentration (291, 280, and 231 nm, respectively). Partial specific volume \( v_{\text{bar}} \) of 0.713 ml/g was computed from the amino acid composition; solvent density = 1.004 g/ml and viscosity = 1.03 centipoise were set from tables. Data analysis was performed with the program Origin (Microcal).

**RESULTS**

**Purification of RCL and Molecular Properties of the Recombinant Proteins**—Both RCL and His-RCL were produced as soluble proteins, and their purity was estimated to be >95% by SDS-PAGE (Fig. 1). The molecular mass of RCL and His-RCL, according to appropriate markers (24–26 kDa), is higher than the deduced 18–20-kDa molecular mass. Electrospray ionization mass spectrometry of RCL is mostly monomeric (free averaged molecular mass 22,603 Da). At 30 \( \mu \)M, His-RCL is at equilibrium between monomeric (20,440 Da) and dimeric (40,880 Da) states (Fig. 2). The dissociation constant \( K_d \) of 2 evenly spread over 10.40 \( \mu \)M and a variance of 4.76 \( 10^{-4} \). Residual values were below 10 \( ^{-2} \) evenly spread over best fit lines.

RCL at concentrations >1 mg/ml could be stored at −20 °C for at least 1 year without loss of activity. RCL is a heat-stable protein, as the temperature of half denaturation (Tm) was estimated to be ~74 °C.

**The Rationale for Identifying the Catalytic Function of RCL**—Examination of the homology of RCL with N-deoxyribosyltransferase from Lactobacillus revealed several interesting features (Fig. 3). Several amino acids that participate in the active site of Lactobacillus leichmannii N-deoxyribosyltransferase are conserved in RCL, such as the Glu-105, which is also involved in a hydrogen bond with the 3′-OH of the sugar of the deoxyriboside (16). Tyr-2, which stabilizes this bond, as well as Asp-75, involved in the binding of the base, are also conserved. Interestingly, the two amino acids, Asp-99 and Asn-172, involved in the binding of the 5′-OH of the sugar, are not conserved in RCL, being replaced by two Ser residues with smaller size (Fig. 3, inset). We hypothesized that the substrate recognized by RCL should be related to deoxyribonucleosides (substrate of N-deoxyribosyltransferase) or the corresponding phosphorylated compounds. Consequently, ~50 ribonucleosides and deoxyribonucleosides, including their mono-, di-, and triphosphate derivatives, were incubated individually for several hours at 37 °C with pure RCL, and then the reaction products were analyzed by thin layer chromatography and later by HPLC (Fig. 4). When RCL was incubated with various deoxyribonucleoside 5′-monophosphates (and to a lesser extent with deoxyribonucleoside diphosphates), a constant reaction product was the corresponding free base. We deduced that RCL catalyzes the following hydrolytic reaction: deoxyribonucleoside 5′-monophosphate (dNMP) + \( \text{H}_2\text{O} \) → free base (N) + deoxyribose 5-phosphate (dR5P). The existence of the two reaction products in stoichiometric amounts was demonstrated by using dIMP as a substrate and identifying enzymatically the end prod-
ucts, hypoxanthine and deoxyribose 5-phosphate, as described under “Experimental Procedures.” No deoxyribose 5-phosphate transfer was detected, whether dCMP or dGMP was the donor or any base was the acceptor. In addition, no dNMP was synthesized when RCL was incubated in the presence of deoxyribose 5-phosphate and guanine (data not shown). We concluded that RCL cleaves the N-glycosidic bond of deoxynucleoside 5'-monophosphate to liberate deoxyribose 5-phosphate and the free base and that this reaction is not reversible. Hence, we found a previously undescribed enzyme, deoxynucleoside 5'-monophosphate N-glycosidase, that is encoded by Rcl, a Myc target with tumorigenic potential.

Catalytic Properties of the Recombinant Proteins—With saturating concentrations of dGMP or dCMP, RCL showed an optimum pH value of 6.0. 50% of the maximal activity was still observed at pH 7.0 in the case of dCMP, whereas it was only 20%
in the case of dGMP. In both cases at pH 8.0, only 10% of the enzyme activity remained. Several metals were tested for their ability to stimulate or inhibit the reaction, Ca$^{2+}$, Mg$^{2+}$, Zn$^{2+}$, Na$^+$, and K$^+$. Only Zn$^{2+}$ inhibited the reaction, whereas the other metals had no effect. Initial velocity experiments were carried out at variable concentrations of the six deoxynucleoside 5'-monophosphate: dAMP, dCMP, dGMP, dIMP, dTMP, and dTMP (Table 1). The kinetic parameters with dGMP indicate that RCL is a typical Michaelian enzyme with a $K_{m}$ value of 50 $\mu$M and a $V_{max}$ of 0.09 units mg$^{-1}$, which correspond to a $k_{cat}$ of 0.0268 s$^{-1}$. Purine deoxynucleotides have a better affinity for RCL than pyrimidine deoxynucleotides. The $K_{m}$ value of RCL for dCMP (4 mM), dUMP (15 mM), and dTMP (>50 mM) are high as compared with dGMP (50 $\mu$M), dAMP (250 $\mu$M), and dIMP (450 $\mu$M). The $k_{cat}/K_{m}$ measure of substrate efficiency also indicates a preference for purine deoxynucleotides. RCL cleaves dGMP 20 times more efficiently than dAMP and 40 times more than dIMP. $k_{cat}/K_{m}$ and $K_{m}$ of RCL for dGMP (619 M$^{-1}$s$^{-1}$ and 48 $\mu$M) are comparable with that reported for the related nucleotide hydrolase BlsM from *Streptomyces griseochromogenes* for dCMP (146 M$^{-1}$s$^{-1}$ and 65 $\mu$M) (24).

To better understand the catalytic mechanism of RCL, several compounds were tested as the substrate or inhibitor of the enzyme activity. The initial velocity of the reaction was measured either at a variable concentration of dGMP, both in the absence and presence of inhibitors, or at fixed a concentration of dGMP and variable concentrations of inhibitors, allowing the testing of the nature of the inhibition. The double reciprocal plot confirms that GMP and 6-methylthio-GMP are competitive inhibitors for dGMP with a $K_{i}$ value of 20 and 10 $\mu$M, respectively. Thus, the presence of an OH at the 2' position of the sugar has a critical influence. The position of the phosphate is also important, as 2'-deoxyguanosine 3'-monophosphate is neither a substrate nor an inhibitor of RCL. The presence of an oxo at position 8 of the base is sufficient to modify the recognition by RCL, as 8-oxo-dGMP is neither a substrate nor an inhibitor.

**Kinetic Parameters of RCL E105A Mutant**—The similarity of the amino acids sequence and the similarity of reaction between RCL and N-deoxyribosyltransferase led us to investigate the catalytic mechanism. The Glu-105 was chosen for site-directed mutagenesis, because it is the active site nucleophile in *L. leichmannii* N-deoxyribosyltransferase (16, 17) and because of its conservation in the different N-deoxyribosyltransferase-like sequences (Fig. 3). The Glu-105 mutated to Ala in RCL (Table 2) has a profound effect on the $K_{m}$ value, which is enhanced by a factor of 170, whereas the $V_{max}$ value remains in the same order of magnitude. It was thus concluded that Glu-105 may be involved in the substrate binding but is not

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**TABLE 1**

| Nucleotide | $k_{cat}$ | $K_{m}$ | $k_{cat}/K_{m}$ |
|------------|----------|--------|----------------|
| dGMP       | 0.0297   | 48     | 619            |
| dAMP       | 0.0066   | 250    | 26.4           |
| dIMP       | 0.0066   | 450    | 14.7           |
| dCMP       | 0.0231   | 4000   | 5.8            |
| dUMP       | 0.158    | 15600  | 10.1           |
| dTMP       | ND       | ND     | <0.14          |

**TABLE 2**

| Enzyme   | $k_{cat}$ | $K_{m}$ | $k_{cat}/K_{m}$ |
|----------|-----------|--------|----------------|
| Wild-type | 0.0297    | 48     | 619            |
| E105A variant | 0.0178 | 5000   | 3.6            |

FIGURE 4. Formation of hypoxanthine following incubation of RCL with deoxyinosine 5'-monophosphate. A, HPLC chromatogram of deoxyinosine 5'-monophosphate (dIMP). B, HPLC chromatogram of hypoxanthine (Hx). C, HPLC chromatogram of deoxyinosine (dI). D, HPLC chromatogram of RCL assay products with deoxyinosine 5'-monophosphate as substrate. Retention times are indicated next to each peak. E and F correspond to the UV spectra from 210 to 400 nm of the hypoxanthine peak of B and of the product of the reaction from D, respectively (indicated by an asterisk).
the catalytic amino acid as found in L. leichmannii N-deoxyribosyltransferase.

DISCUSSION

With increasing numbers of genome sequences available, functional prediction of open reading frames is a significant advance, but defining precise functions of novel open reading frames remains a challenge despite sequence homology to known functional domains. For example, the clustering of orthologous groups (COGs) that brought together comparative genomics and protein classification has allowed the automatic functional annotation of genes and proteins (18). Orthologs most often have equivalent functions, and COG 3613 illustrates all of the proteins with a conserved domain with N-deoxyribosyltransferase. In COG 3613, only two crystal structures of N-deoxyribosyltransferases in the presence of different ligands were described (16, 19). These structures allowed the determination of the amino acid residues important in substrate binding and catalysis and also explained the substrate specificity. Knowing this, we reconsidered the 3613 COG by focusing our interest on RCL. RCL was chosen for several reasons: (i) it was the more distant protein in the COG, (ii) its function was unknown, (iii) it was only present in mammals, and (iv) the Rcl gene is a Myc target gene, which is up-regulated in human cancers and has tumorigenic potential. By combining the structural data obtained with L. leichmannii and Lactobacillus helveticus N-deoxyribosyltransferases and the sequence identities of RCL and N-deoxyribosyltransferases, we hypothesized that the two proteins may have related activities with different substrate specificities. The biochemical experiments performed with either pure native RCL or with a His-tagged RCL demonstrated that it codes for a deoxynucleoside 5′-monophosphate glycosidase, a previously undescribed activity. Indeed, N-glycosylhydrolyses with a pyrimidine preference have been described in Neisseria meningitidis (20), Streptomyces virginiensis (21, 22), and S. griseochromogenes (23, 24). On the other hand, ribosylhydrolyses specific for inosine or adenosine 5′-monophosphate were also reported (25, 26). None of them hydrolyze purine deoxynucleoside 5′-monophosphate. The RCL activity seems related to N-deoxyribosyltransferase, because in the absence of an acceptor base, L. leichmannii N-deoxyribosyltransferase catalyzes the hydrolysis of deoxynucleosides (27). L. leichmannii N-deoxyribosyltransferase is a hexamer in its native state, with one active site/subunit. A complete catalytic center requires the participation from a neighboring subunit, indicating that oligomerization is necessary for catalysis (16). Molecular mass measurement shows that RCL is in a monomer-dimer equilibrium. It is notable that RCL (C6orf108) also dimerizes intracellularly in the yeast two-hybrid assay (5). Considering the RCL concentration used and the tendency of RCL to aggregate at high concentration, it is likely that RCL is active as a monomer in the catalysis conditions explored in vitro; however, whether its activity requires a dimeric state in vivo is not known. Thus, the quaternary structure of RCL should be different from that of L. leichmannii N-deoxyribosyltransferase, which exists as a hexamer.

The difference of substrate specificity (deoxynucleosides versus deoxynucleosides 5′-monophosphate) between N-deoxyri-

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FIGURE 5. Possible functional roles of RCL as a previously undescribed deoxynucleoside 5′-monophosphate N-glycosidase. RCL cleaves a deoxynucleoside 5′-monophosphate (dNMP) to liberate the free base N and deoxyribose 5-phosphate. The free base N can be recycled through the purine or pyrimidine salvage pathways. Deoxyribose 5-phosphate can be converted to glyceraldehyde 3-phosphate and acetaldehyde by deoxyribose 5-phosphate aldolase. Glyceraldehyde 3-phosphate can be converted to lactate through glycolysis and acetaldehyde converted to acetyl-CoA by aldehyde oxidase and acetyl-CoA synthetase. Deoxyribose 5-phosphate could be converted to deoxyribose by phosphatase, which in turn would stimulate tumor growth and angiogenesis.

Another possibility could be the requirement of supplementary energy for the tumor cells, and deoxyribose 5-phosphate could substitute or supplement glucose in aerobic and anaerobic conditions. Indeed, deoxyribose 5-phosphate can be converted by deoxyribose 5-phosphate aldolase into acetaldehyde and glyceraldehyde 3-phosphate that is further catalyzed to lactate.

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through glycolysis, whereas acetaldehyde would be converted into acetyl-CoA (Fig. 5). In addition, deoxyribose 5-phosphate could be dephosphorylated into deoxyribose. Deoxyribose has both chemotactic and angiogenic activity (30). It also inhibits a hypoxia-induced apoptotic pathway. Furthermore, deoxyribose was shown to enhance the level of expression of the angiogenic factor, vascular endothelial growth factor (30). This could be related to the fact that RCL has transforming activity when coexpressed with vascular endothelial growth factor (10). Thymidine phosphorylase, which catalyzes the conversion of thymidine to thymine and deoxyribose 1-phosphate, has been known to be angiogenic through deoxyribose and hence is also known as endothelial cell growth factor 1 (30). In this regard, RCL and thymidine phosphorylase participate in nucleotide metabolism and putatively couple metabolism to intercellular signaling through deoxyribose. In aggregate, the novel catalytic activity of RCL defined here along with the reported activities of the deoxyribose 5-phosphate reveal potential roles for RCL in tumorigenesis. Hence, RCL could be a good target for the development of anti-tumor and or anti-angiogenesis drugs. Further studies of the role in vivo of RCL will contribute to better understanding of its physiological role in normal and pathological role in cancerous cells.

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