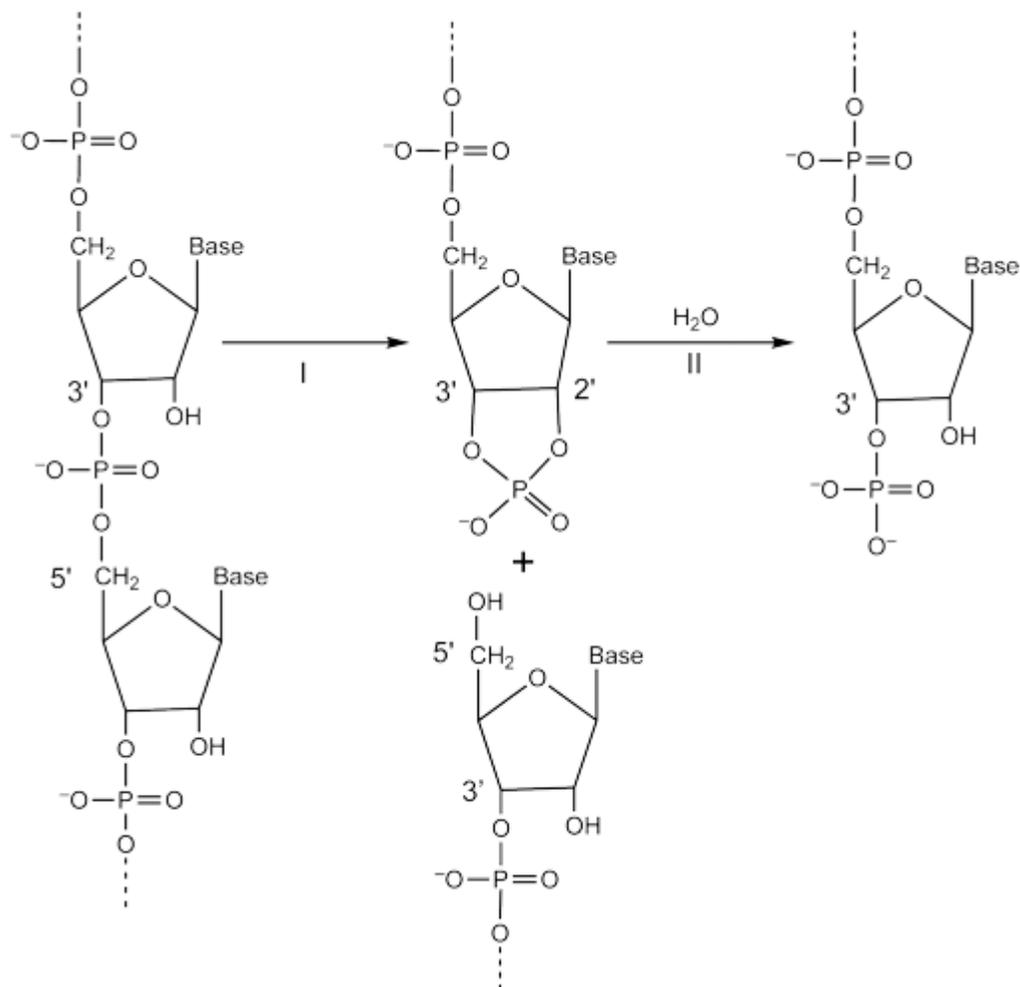


## Ribonuclease classification (October 2018)

[Prepared by Keith Tipton]

The classification of the ribonucleases has been a matter of some contention. Whereas some appear to act as simple hydrolases, cleaving the 3',5'-phosphatodiester bonds linking adjacent nucleotides, others, such as pancreatic ribonuclease, cleave to give a 2',3'-cyclophosphate derivative, which is subsequently hydrolysed to the 3'-phosphate, as shown below.



Pancreatic ribonuclease was listed among those enzymes transferring phosphate groups, *Enzymes catalysing other phosphate-transfer reactions*, as entry 502 in the Table of Enzymes published by Dixon & Webb in 1958 [1]. When the Enzyme List was formally divided into specific reaction classes, it was listed as a transferase, (EC 2.7.7.16) in 1961 [2], but, since the overall reaction was hydrolysis, it was reclassified as a hydrolase (EC 3.1.27.5) in 1972 [3]. However, it became clear that neither of these classification types adequately described the activity of this enzyme. The cyclophosphate produced in reaction I is actually released from the enzyme and the subsequent hydrolytic step (reaction II), which occurs by a reversal of reaction I with the hydroxyl group of water replacing the 5'-hydroxyl group of ribose, only occurring to any appreciable extent when the formation of the cyclophosphate product is essentially complete. Thus the reaction may be regarded as that of a lyase (a phosphorous-oxygen lyase) since it 'cleaves bonds by means other than by hydrolysis or oxidation'. This is the class of enzyme where two (or more) substrates are involved in one reaction direction, but there is one compound fewer in the

other direction and when acting on the single substrate, a molecule is eliminated and this generates either a new double bond or, in this case, a new ring structure.

Because of this, pancreatic ribonuclease and some other ribonucleases have now been reclassified as phosphorous-oxygen lyases (EC 4.6.1.-). Those ribonucleases which appear to behave as simple hydrolases remain in EC 3 along with the DNases, which cannot form 2',3'-cyclophosphate products.

1. Dixon M. & Webb EC. (1958) *Enzymes*, Longmans Green, London, pp. 185–227.
2. Report of the Commission on Enzymes of the International Union of Biochemistry (1961). Pergamon Press, New York & London.
3. Enzyme Nomenclature (1973) Recommendations (1972) of the Commission on Biochemical Nomenclature on the Nomenclature and Classification of Enzymes, Together with their Units and the Symbols of Enzyme Kinetics. Elsevier, Amsterdam.