

Rational Proteomics: Substrate Specific Fingerprints in SCOR Enzymes. W. Duax^{1,3}, L. Habegger¹, R. Huether¹, V. Pletnev²,
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The short-chain oxidoreductase (SCOR) family of enzymes is an ancient family that includes many steroid dehydrogenases vital to growth and development. A search for covariance among residues predicted to line the substrate binding pocket in SCOR enzymes led to the identification of nine sequence positions in three loops of the proteins that define the substrate binding pocket. These three loops are found in a 100 residue region of the C-terminal half of SCOR proteins. One combination of amino acids in the nine positions defines the substrate binding site of β -ketoacyl [acyl carrier protein] reductase. Different combinations of amino acids in the same nine sequence positions define the binding sites for eleven different substrates. The table illustrates the eight substrate fingerprints that differ most from one another. Bold letters indicate site specific amino acids common to more than one substrate fingerprint. Some sequence positions are more substrate specific (91 and 93) than others (148 and 193). The substrate fingerprints of the other three subfamilies of SCOR enzymes have different combinations of amino acids in some of these positions. For example, with three residue changes [N146Q, F184Y, and T190V] the fingerprint for β -keto ACPR becomes the fingerprint for aceto-acetyl CoA reductase, enzymes having common substrates but different products.

Structure	Sequence Position										overlap
	#	91	93	146	148	149	184	189	190	193	
I	177	T	D	N	G	Q	F	M	T	L	5
II	24	I	R	G	R	V	Y	N	T	L	3
III	30	Q	V	S	G	K	Y	L	V	Q	3
IV	14	E	P	W	L	F	A	I	N	K	1
V	21	A	A	Q	G	Q	L,I	M,L	L	L	3
VI	19	L	M,L	R	G	M	S	M	Q	L	3
VII	27	S	G	V	L	G	Y	M	A	V	2
VIII	10	N	F	S	G	F	L	F	S	L	3

I. β -keto-acyl ACPR. II. 2-deoxygluconate-3-dehydrogenase (Dh). III. D- β hydroxybutyrate Dh. IV. Glucose-Dh. V. 3-hydroxy CoA Dh. VI. 2,3-dihydroxybenzoate Dh. VII. Polyketide keto reductase. VIII. Retinol Dh.

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