

Supplemental Information - Supplementary Tables S1-S7

**Table S1. Prostate microRNA expression profiling in Zn-deficient middle-aged (11-mo-old) vs Zn-deficient young-adult (2.5-mo-old) rats (Sprague-Dawley strain) using the nanoString™ nCounter rat miRNA expression assay kit (cut off:  $P < 0.05$ , fold-change  $\geq 1.4$ ; n = 6 rats/group)**

miRNA name	Lateral prostate		Fold-change	P-value	*Similarly up- or downregulated in human PCa	References
	(Average counts $\pm$ standard deviation)					
	Zn-deficient middle-aged	Zn-deficient young-adult				
<b>36 upregulated</b>						
miR-290 (human ortholog *miR-373)	968 $\pm$ 229	99 $\pm$ 112	<b>9.79</b>	0.000008	upregulated	(1)
miR-29b	2697 $\pm$ 717	835 $\pm$ 362	<b>3.23</b>	0.000204		
*miR-200c	1687 $\pm$ 373	622 $\pm$ 192	<b>2.71</b>	0.000099	upregulated	(2, 3)
*miR-21	6173 $\pm$ 3255	2317 $\pm$ 718	<b>2.66</b>	0.032911	upregulated	(4)
*miR-22	2135 $\pm$ 312	882 $\pm$ 184	<b>2.42</b>	0.000007	upregulated	(5)
*miR-141	1258 $\pm$ 85	523 $\pm$ 150	<b>2.41</b>	0.000001	upregulated	(6)
<b>*# miR-96</b>	942 $\pm$ 173	396 $\pm$ 173	<b>2.38</b>	0.000278	upregulated	(7, 8)
*miR-375	540 $\pm$ 179	230 $\pm$ 38	<b>2.35</b>	0.007368	upregulated	(2, 7, 8)
*miR-200b	3859 $\pm$ 484	1704 $\pm$ 475	<b>2.26</b>	0.000015	upregulated	(3)
miR-29c	4043 $\pm$ 860	1793 $\pm$ 441	<b>2.25</b>	0.000198	-	
*miR-200a	11819 $\pm$ 3004	5265 $\pm$ 2025	<b>2.24</b>	0.001272	upregulated	(9)
miR-672	48 $\pm$ 12	21 $\pm$ 7	<b>2.24</b>	0.00101	-	
miR-741-3p	61 $\pm$ 23	29 $\pm$ 11	<b>2.12</b>	0.010257	-	
miR-148b-3p	273 $\pm$ 61	133 $\pm$ 53	<b>2.05</b>	0.001756	-	
miR-30b-5p	1065 $\pm$ 251	535 $\pm$ 282	<b>1.99</b>	0.006358	-	
miR-146a	313 $\pm$ 59	162 $\pm$ 41	<b>1.93</b>	0.000466	-	
miR-429	3335 $\pm$ 410	1794 $\pm$ 364	<b>1.86</b>	0.000043	-	
miR-1224	53 $\pm$ 12	29 $\pm$ 7	<b>1.85</b>	0.001685	-	
<b>*# miR-182</b>	34 $\pm$ 12	20 $\pm$ 8	<b>1.73</b>	0.029198	upregulated	(2, 7, 8)
miR-34a	48 $\pm$ 11	28 $\pm$ 6	<b>1.72</b>	0.003222	-	
*miR-30d	1214 $\pm$ 183	705 $\pm$ 172	<b>1.72</b>	0.000561	upregulated	(10)
miR-653	11 $\pm$ 3	7 $\pm$ 2	<b>1.63</b>	0.019231	-	
miR-142-3p	401 $\pm$ 106	247 $\pm$ 40	<b>1.62</b>	0.007488	-	
miR-29a	8494 $\pm$ 1324	5236 $\pm$ 1059	<b>1.62</b>	0.000834	-	
miR-101a	208 $\pm$ 29	130 $\pm$ 23	<b>1.6</b>	0.000415	-	
miR-448	31 $\pm$ 3	20 $\pm$ 9	<b>1.58</b>	0.0287	-	
*miR-222	49 $\pm$ 15	31 $\pm$ 6	<b>1.57</b>	0.021055	upregulated	(11)

miR-365	259 ± 64	166 ± 54	<b>1.56</b>	0.020649	-	
miR-152	726 ± 182	465 ± 99	<b>1.56</b>	0.011547	-	
miR-425	58 ± 5	39 ± 13	<b>1.51</b>	0.00643	-	
let-7b	5125 ± 334	3536 ± 497	<b>1.45</b>	0.000069	-	
let-7a	3446 ± 332	2383 ± 449	<b>1.45</b>	0.000885	-	
miR-511	46 ± 7	32 ± 7	<b>1.42</b>	0.006396	-	
miR-223	46 ± 10	32 ± 6	<b>1.41</b>	0.015748	-	
*miR-32	88 ± 2	63 ± 10	<b>1.41</b>	0.001042	upregulated	(2)
<b>*# miR-183</b>	96 ± 11	68 ± 16	<b>1.41</b>	0.005506	upregulated	(7, 8)
<b>29 downregulated</b>						
miR-127	33 ± 19	168 ± 119	<b>-5</b>	0.038745	-	
*miR-495	17 ± 8	56 ± 33	<b>-3.23</b>	0.032971	downregulated	(12)
miR-433	13 ± 2	36 ± 18	<b>-2.86</b>	0.025546	-	
miR-181c	22 ± 4	52 ± 15	<b>-2.38</b>	0.004144	-	
miR-411	17 ± 5	39 ± 10	<b>-2.27</b>	0.000658	-	
miR-431	13 ± 3	29 ± 11	<b>-2.22</b>	0.015275	-	
miR-134	19 ± 7	35 ± 7	<b>-1.89</b>	0.002102	-	
miR-369-5p	14 ± 3	26 ± 6	<b>-1.85</b>	0.001239	-	
miR-300-3p	11 ± 5	20 ± 6	<b>-1.82</b>	0.023012	-	
*miR-199a-3p	874 ± 310	1603 ± 571	<b>-1.82</b>	0.020597	downregulated	(13)
*miR-132	24 ± 4	43 ± 14	<b>-1.79</b>	0.0186	downregulated	(14)
miR-199a-5p	513 ± 166	901 ± 233	<b>-1.75</b>	0.007737	-	
*miR-376c	27 ± 9	47 ± 16	<b>-1.72</b>	0.025688	downregulated	(12)
*miR-100	219 ± 60	363 ± 55	<b>-1.67</b>	0.001511	downregulated	(15)
miR-326	32 ± 10	53 ± 9	<b>-1.67</b>	0.003441	-	
miR-873	8 ± 2	13 ± 3	<b>-1.59</b>	0.012127	-	
miR-181a	539 ± 228	852 ± 133	<b>-1.59</b>	0.01573	-	
miR-25	424 ± 47	673 ± 166	<b>-1.59</b>	0.013094	-	
miR-539	37 ± 7	59 ± 16	<b>-1.59</b>	0.014177	-	
miR-328a	38 ± 7	59 ± 15	<b>-1.56</b>	0.011051	-	
*miR-17-5p	108 ± 24	168 ± 45	<b>-1.56</b>	0.015873	downregulated	(4)
*miR-130a	343 ± 99	526 ± 70	<b>-1.54</b>	0.004178	downregulated	(16)
miR-379	15 ± 4	23 ± 6	<b>-1.54</b>	0.024061	-	
miR-874	10 ± 3	15 ± 3	<b>-1.47</b>	0.015069	-	
miR-301a	45 ± 10	66 ± 15	<b>-1.45</b>	0.021539	-	
miR-153	19 ± 6	28 ± 5	<b>-1.45</b>	0.023759	-	
*miR-409-3p	15 ± 2	21 ± 4	<b>-1.45</b>	0.002277	downregulated	(17)
*miR-27b	1852 ± 461	2630 ± 478	<b>-1.43</b>	0.016723	downregulated	(18)
miR-342-3p	53 ± 14	74 ± 11	<b>-1.41</b>	0.016961	-	

\*# denotes the entire miR-183-96-182 cluster that is overexpressed in human prostate cancer and regulates Zn-homeostasis is upregulated in Zn-deficient vs Zn-sufficient middle-aged rat prostate

**Table S2. Prostate microRNA expression profiling in Zn-sufficient middle-aged (11-mo-old) vs Zn-sufficient young adult (2.5-mo-old) rats (Sprague-Dawley strain) using the nanoString™ nCounter rat miRNA expression assay kit (cut off:  $P < 0.05$ , fold-change  $\geq 1.4$ ; n = 6 rats/group)**

miRNA name	Lateral prostate		Fold-change	P-value	*Similarly up- or downregulated in human PCa	References
	(Average counts $\pm$ standard deviation)					
	Zn-Sufficient middle-aged	Zn-Sufficient young-adult				
<b>38 upregulated</b>						
miR-290 (human ortholog *miR-373)	638 $\pm$ 226	103 $\pm$ 75	<b>6.17</b>	0.001455	upregulated	(1)
*miR-200a	11573 $\pm$ 1820	3928 $\pm$ 1071	<b>2.95</b>	0.000005	upregulated	(9)
*miR-200c	1590 $\pm$ 226	584 $\pm$ 120	<b>2.72</b>	0.000002	upregulated	(2, 3)
miR-29b	2142 $\pm$ 314	869 $\pm$ 94	<b>2.46</b>	0.000087	-	
*miR-141	1118 $\pm$ 187	485 $\pm$ 45	<b>2.31</b>	0.000279	upregulated	(6)
*miR-375	562 $\pm$ 98	245 $\pm$ 58	<b>2.3</b>	0.000045	upregulated	(2, 7, 8)
*miR-200b	3798 $\pm$ 504	1786 $\pm$ 388	<b>2.13</b>	0.000016	upregulated	(3)
miR-672	54 $\pm$ 15	26 $\pm$ 4	<b>2.10</b>	0.00506	-	
miR-3564	20 $\pm$ 3	10 $\pm$ 4	<b>2.00</b>	0.000496	-	
miR-29c	3406 $\pm$ 559	1725 $\pm$ 245	<b>1.97</b>	0.000051	-	
miR-30b-5p	889 $\pm$ 188	460 $\pm$ 94	<b>1.93</b>	0.000539	-	
*miR-144	70 $\pm$ 26	39 $\pm$ 10	<b>1.82</b>	0.018764	upregulated	(1)
miR-291b	15 $\pm$ 6	8 $\pm$ 3	<b>1.81</b>	0.029774	-	
<b>*miR-96</b>	792 $\pm$ 93	443 $\pm$ 122	<b>1.79</b>	0.000239	upregulated	(7)
*miR-30d	1094 $\pm$ 241	617 $\pm$ 70	<b>1.77</b>	0.003763	upregulated	(10)
miR-148b-3p	256 $\pm$ 39	150 $\pm$ 32	<b>1.70</b>	0.000398	-	
miR-292-3p	18 $\pm$ 6	11 $\pm$ 4	<b>1.59</b>	0.035223	-	
miR-30e	206 $\pm$ 50	129 $\pm$ 21	<b>1.59</b>	0.005951	-	
miR-34a	41 $\pm$ 4	26 $\pm$ 4	<b>1.57</b>	0.000092	-	
miR-511	48 $\pm$ 10	31 $\pm$ 2	<b>1.56</b>	0.007412	-	
miR-207	13 $\pm$ 3	8 $\pm$ 2	<b>1.54</b>	0.007199	-	
miR-298	21 $\pm$ 3	14 $\pm$ 2	<b>1.54</b>	0.000971	-	
miR-3578	58 $\pm$ 18	38 $\pm$ 9	<b>1.53</b>	0.030298	-	
miR-190b	24 $\pm$ 8	16 $\pm$ 5	<b>1.51</b>	0.044389	-	
miR-201	33 $\pm$ 5	22 $\pm$ 5	<b>1.49</b>	0.005412	-	
*miR-31	28 $\pm$ 7	19 $\pm$ 3	<b>1.48</b>	0.014426	upregulated	(2)
*miR-21	3763 $\pm$ 369	2554 $\pm$ 181	<b>1.47</b>	0.000029	upregulated	(4)
miR-3589	55 $\pm$ 10	37 $\pm$ 7	<b>1.47</b>	0.004552	-	
*miR-222	39 $\pm$ 4	27 $\pm$ 4	<b>1.47</b>	0.000349	upregulated	(11)
*miR-32	80 $\pm$ 13	55 $\pm$ 11	<b>1.46</b>	0.00448	upregulated	(2)
miR-29a	6956 $\pm$ 1253	4775 $\pm$ 485	<b>1.46</b>	0.002617	-	
miR-2964	14 $\pm$ 3	10 $\pm$ 1	<b>1.45</b>	0.005915	-	
miR-3592	30 $\pm$ 8	21 $\pm$ 4	<b>1.43</b>	0.030332	-	
miR-883	15 $\pm$ 3	10 $\pm$ 3	<b>1.43</b>	0.041527	-	
miR-429	2820 $\pm$ 443	1977 $\pm$ 289	<b>1.43</b>	0.002927	-	
miR-3594-3p	74 $\pm$ 6	52 $\pm$ 9	<b>1.42</b>	0.000467	-	
miR-628	86 $\pm$ 17	61 $\pm$ 8	<b>1.41</b>	0.008299	-	
miR-101a	182 $\pm$ 38	130 $\pm$ 32	<b>1.4</b>	0.0298	-	

<b>46 downregulated</b>						
miR-376b-3p	25 ± 10	94 ± 50	<b>-3.71</b>	0.01991	-	
miR-127	41 ± 22	137 ± 81	<b>-3.38</b>	0.03212	-	
miR-218a	86 ± 45	285 ± 173	<b>-3.31</b>	0.03651	-	
miR-369-3p	21 ± 9	66 ± 29	<b>-3.09</b>	0.01077	-	
miR-434	44 ± 14	130 ± 58	<b>-2.97</b>	0.01356	-	
*miR-487b	13 ± 5	37 ± 20	<b>-2.88</b>	0.02826	downregulated	(12)
*miR-124	27 ± 18	72 ± 39	<b>-2.63</b>	0.02984	downregulated	(19)
miR-410	24 ± 5	57 ± 25	<b>-2.42</b>	0.02096	-	
*miR-199a-3p	829 ± 133	1983 ± 314	<b>-2.39</b>	0.00001	downregulated	(13)
miR-382	23 ± 10	50 ± 26	<b>-2.18</b>	0.04019	-	
*miR-130a	298 ± 63	638 ± 105	<b>-2.14</b>	0.00005	downregulated	(16)
miR-196a	32 ± 7	65 ± 25	<b>-2.03</b>	0.02259	-	
*miR-100	210 ± 40	416 ± 90	<b>-1.98</b>	0.00045	downregulated	(20)
miR-181a	431 ± 95	848 ± 163	<b>-1.97</b>	0.00030	-	
miR-411	19 ± 6	37 ± 12	<b>-1.90</b>	0.00948	-	
miR-15b	210 ± 27	394 ± 121	<b>-1.88</b>	0.01224	-	
miR-136	28 ± 7	52 ± 21	<b>-1.87</b>	0.03728	-	
miR-199a-5p	466 ± 117	857 ± 96	<b>-1.84</b>	0.00008	-	
miR-450a	68 ± 11	123 ± 15	<b>-1.81</b>	0.00003	-	
miR-1949	22 ± 8	40 ± 13	<b>-1.79</b>	0.02032	-	
miR-340-5p	45 ± 9	80 ± 13	<b>-1.78</b>	0.00031	-	
*miR-495	22 ± 7	38 ± 15	<b>-1.77</b>	0.03376	downregulated	(12)
miR-323	29 ± 8	51 ± 13	<b>-1.77</b>	0.00521	-	
*miR-27b	1648 ± 509	2907 ± 681	<b>-1.76</b>	0.00464	downregulated	(18)
miR-667	11 ± 5	19 ± 4	<b>-1.73</b>	0.01195	-	
*miR-376c	27 ± 5	47 ± 13	<b>-1.70</b>	0.00705	downregulated	(12)
*miR-133a	59 ± 7	100 ± 22	<b>-1.69</b>	0.00488	downregulated	(21)
miR-872	45 ± 7	74 ± 10	<b>-1.66</b>	0.00015	-	
miR-299	8 ± 2	13 ± 1	<b>-1.65</b>	0.00012	-	
*miR-99a	1833 ± 303	2984 ± 368	<b>-1.63</b>	0.00015	downregulated	(22)
miR-301a	47 ± 10	77 ± 12	<b>-1.63</b>	0.00093	-	
miR-196c	70 ± 16	113 ± 35	<b>-1.61</b>	0.02193	-	
miR-181c	28 ± 6	44 ± 8	<b>-1.59</b>	0.00320	-	
miR-326	31 ± 9	50 ± 10	<b>-1.59</b>	0.00540	-	
*miR-181b+miR-181d	18 ± 5	28 ± 6	<b>-1.56</b>	0.01147	downregulated	(7)
miR-342-3p	48 ± 11	75 ± 14	<b>-1.56</b>	0.00404	-	
miR-25	370 ± 46	577 ± 100	<b>-1.56</b>	0.00097	-	
miR-539	37 ± 6	57 ± 14	<b>-1.52</b>	0.01234	-	
miR-337	17 ± 6	25 ± 3	<b>-1.52</b>	0.00938	-	
miR-125a-5p	603 ± 61	917 ± 181	<b>-1.52</b>	0.00661	-	
let-7e	319 ± 57	466 ± 81	<b>-1.46</b>	0.00451	-	
*miR-17-5p	106 ± 18	154 ± 22	<b>-1.46</b>	0.00215	downregulated	(4)
miR-322	83 ± 13	118 ± 19	<b>-1.43</b>	0.00319	-	
miR-27a	447 ± 82	632 ± 107	<b>-1.41</b>	0.00723	-	
miR-9	81 ± 12	115 ± 11	<b>-1.41</b>	0.00058	-	
miR-431	20 ± 3	28 ± 7	<b>-1.41</b>	0.03986	-	

**Table S3. Prostate microRNA expression profiling in Zn-deficient adult (5-mo-old) vs Zn-deficient young-adult (2.5-mo-old) rats (Sprague-Dawley strain) using the nanoString™ nCounter rat miRNA expression assay kit (cut off:  $P < 0.05$ , fold-change  $\geq 1.4$ ;  $n = 6$  rats/group)**

miRNA name	Lateral prostate (Average counts $\pm$ standard deviation)		Fold-change	P-value	*Similarly up- or downregulated in human PCa	References
	Zn-deficient adult	Zn-deficient young adult				
<b>25 upregulated</b>						
miR-290 (human ortholog *miR-373)	329 $\pm$ 123	99 $\pm$ 112	3.33	0.006899	upregulated	(1)
miR-29b	2000 $\pm$ 496	835 $\pm$ 362	2.39	0.000913	-	
miR-741-3p	55 $\pm$ 11	29 $\pm$ 11	1.90	0.001919	-	
miR-196c	130 $\pm$ 34	70 $\pm$ 12	1.85	0.005661	-	
<b>*miR-96</b>	727 $\pm$ 111	396 $\pm$ 173	1.84	0.002734	upregulated	(7)
*miR-22	1607 $\pm$ 240	882 $\pm$ 184	1.82	0.000154	upregulated	(5)
miR-148b-3p	241 $\pm$ 36	133 $\pm$ 54	1.81	0.002247	-	
miR-7b	42 $\pm$ 8	24 $\pm$ 5	1.73	0.000953	-	
miR-543	131 $\pm$ 16	76 $\pm$ 28	1.73	0.001996	-	
miR-101a	218 $\pm$ 38	130 $\pm$ 23	1.68	0.000637	-	
*miR-200c	1038 $\pm$ 215	622 $\pm$ 192	1.67	0.005359	upregulated	(2, 3)
miR-29c	2952 $\pm$ 747	1793 $\pm$ 441	1.65	0.008375	-	
miR-142-3p	406 $\pm$ 96	247 $\pm$ 40	1.64	0.003893	-	
miR-146a	261 $\pm$ 39	161 $\pm$ 42	1.61	0.001631	-	
miR-295	33 $\pm$ 7	22 $\pm$ 7	1.56	0.022132	-	
*miR-21	3491 $\pm$ 778	2317 $\pm$ 718	1.51	0.021716	upregulated	(4)
miR-30c	286 $\pm$ 45	192 $\pm$ 64	1.49	0.014592	-	
miR-29a	7743 $\pm$ 1195	5236 $\pm$ 1059	1.48	0.003236	-	(23)
miR-33	46 $\pm$ 6	31 $\pm$ 4	1.46	0.000706	-	
<b>*miR-183</b>	99 $\pm$ 15	68 $\pm$ 16	1.45	0.006368	upregulated	(7, 8)
miR-98	369 $\pm$ 54	254 $\pm$ 87	1.45	0.020334	-	
miR-3552	29 $\pm$ 5	20 $\pm$ 4	1.44	0.008956	-	
*miR-26a	333 $\pm$ 60	233 $\pm$ 45	1.43	0.008592	upregulated	(2)
miR-340-5p	86 $\pm$ 20	61 $\pm$ 15	1.42	0.033099	-	
let-7a	3339 $\pm$ 497	2383 $\pm$ 449	1.40	0.005742	-	
<b>9 downregulated</b>						
miR-134	20 $\pm$ 4	35 $\pm$ 7	-1.75	0.001072	-	
miR-219-5p	12 $\pm$ 3	21 $\pm$ 5	-1.67	0.006543	-	
miR-3577	14 $\pm$ 3	23 $\pm$ 7	-1.67	0.010419	-	
miR-541	14 $\pm$ 3	22 $\pm$ 7	-1.59	0.018707	-	
miR-539	38 $\pm$ 12	59 $\pm$ 17	-1.56	0.029863	-	
miR-181c	34 $\pm$ 10	52 $\pm$ 15	-1.54	0.034197	-	
*miR-409-3p	14 $\pm$ 5	21 $\pm$ 4	-1.52	0.013357	downregulated	(17)
miR-3561-3p	32 $\pm$ 7	45 $\pm$ 11	-1.43	0.032973	-	
miR-411	27 $\pm$ 5	39 $\pm$ 10	-1.43	0.026387	-	

**Table S4. Prostate microRNA expression profiling in Zn-sufficient adult (5-mo-old) and Zn-sufficient young-adult (2.5-mo-old) rats (Sprague-Dawley strain) using the nanoString™ nCounter rat miRNA expression assay kit (cut off:  $P < 0.05$ , fold-change  $\geq 1.4$ ;  $n = 6$  rats/group)**

miRNA name	Lateral prostate (Average counts $\pm$ standard deviation)		Fold-change	P-value	*Similarly up- or downregulated in human PCa	References
	Zn-sufficient adult	Zn-sufficient young-adult				
<b>19 upregulated</b>						
miR-301b	23 $\pm$ 5	13 $\pm$ 3	1.73	0.001840	-	
miR-139-3p	21 $\pm$ 6	12 $\pm$ 5	1.69	0.027444	-	
miR-29b	1460 $\pm$ 199	869 $\pm$ 94	1.68	0.000062	-	
*miR-200c	963 $\pm$ 196	584 $\pm$ 120	1.65	0.002391	upregulated	(2, 3)
miR-449c-5p	19 $\pm$ 3	12 $\pm$ 2	1.64	0.000285	-	
miR-3577	33 $\pm$ 5	20 $\pm$ 7	1.64	0.005812	-	
miR-327	27 $\pm$ 7	17 $\pm$ 3	1.62	0.007680	-	
miR-29c	2741 $\pm$ 424	1725 $\pm$ 245	1.59	0.000478	-	
miR-207	13 $\pm$ 4	9 $\pm$ 2	1.59	0.014644	-	
miR-3563-3p	26 $\pm$ 5	16 $\pm$ 4	1.58	0.003346	-	
miR-347	30 $\pm$ 8	19 $\pm$ 9	1.58	0.039193	-	
*miR-375	384 $\pm$ 67	245 $\pm$ 58	1.57	0.003205	upregulated	(2, 7, 8)
miR-3562	17 $\pm$ 4	11 $\pm$ 1	1.55	0.006761	-	
miR-328b-3p	28 $\pm$ 4	19 $\pm$ 7	1.48	0.016967	-	
miR-3585-3p	27 $\pm$ 5	18 $\pm$ 4	1.47	0.010414	-	
miR-298	19 $\pm$ 3	14 $\pm$ 2	1.44	0.002294	-	
miR-876	25 $\pm$ 7	18 $\pm$ 4	1.44	0.036926	-	
*miR-187	38 $\pm$ 7	26 $\pm$ 8	1.43	0.024827	upregulated	(24)
miR-3575	18 $\pm$ 3	13 $\pm$ 3	1.41	0.009606	-	
<b>20 downregulated</b>						
miR-127	37 $\pm$ 15	137 $\pm$ 81	-3.70	0.028938	-	
miR-376b-3p	30 $\pm$ 9	94 $\pm$ 50	-3.13	0.026127	-	
*miR-124	25 $\pm$ 26	72 $\pm$ 39	-2.86	0.035348	downregulated	(19)
miR-434	55 $\pm$ 30	130 $\pm$ 58	-2.38	0.017522	-	
*miR-487b	17 $\pm$ 8	37 $\pm$ 20	-2.22	0.039431	downregulated	(12)
miR-410	27 $\pm$ 6	57 $\pm$ 25	-2.13	0.029732	-	
miR-369-3p	34 $\pm$ 13	66 $\pm$ 29	-1.92	0.032283	-	
*miR-376a	18 $\pm$ 4	33 $\pm$ 11	-1.82	0.021664	downregulated	(12)
miR-26a	140 $\pm$ 60	238 $\pm$ 62	-1.69	0.019105	-	
miR-324-5p	35 $\pm$ 6	58 $\pm$ 12	-1.67	0.001608	-	
miR-337	15 $\pm$ 4	25 $\pm$ 3	-1.67	0.000416	-	
miR-98	189 $\pm$ 52	301 $\pm$ 106	-1.59	0.042288	-	
miR-543	54 $\pm$ 13	85 $\pm$ 29	-1.56	0.037008	-	

*miR-376c	31 ± 7	47 ± 13	-1.52	0.025441	downregulated	(12)
miR-323	34 ± 7	51 ± 13	-1.52	0.017184	-	
miR-129	13 ± 2	20 ± 6	-1.52	0.030992	-	
miR-99b	185 ± 42	281 ± 58	-1.52	0.008515	-	
miR-539	37 ± 3	57 ± 14	-1.52	0.020555	-	
miR-7b	21 ± 5	30 ± 4	-1.43	0.006742	-	
miR-326	35 ± 5	50 ± 10	-1.43	0.006966	-	

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**Table S5. Metabolomic signature in Zn-deficient young-adult rat prostate**

Metabolites	Median fold-change (Zn-deficient vs sufficient)	<i>P</i> value	Biological process
<b>Downregulated</b> (n = 2)			
Pipecolinic acid	-1.79	0.0230	---
Adenine	-1.69	0.0241	Purine metabolism
<b>Upregulated</b> (n = 3)			
3,6-Anhydro-D-galactose	2.27	0.0000	---
Myo-inositol	1.61	0.0047	Galactose/lipid metabolism
*Uracil	1.47	0.0178	Pyrimidine metabolism

Untargeted metabolomic profiling was by gas chromatography time-of-flight mass spectrometry (n = 8 rats/group). Five significantly dysregulated metabolites ( $P < 0.05$ ) were identified in lateral prostates of Zn-deficient vs sufficient young-adult rat (2.5-mo-old)(Sprague-Dawley strain).

\*Uracil is similarly upregulated in human prostate cancer.

Table S6. Compound\_ChemRICH in Zn-deficient vs Zn-sufficient middle-aged rat prostates (Wistar-Unilever strain)

Compound.Name	InChiKeys	Pubchem.ID	SMILES	pvalue	foldchange	CID	ClusterNumber	xlogp	ClusterLabel	TreeLabel: FDR
xylose	SRBFZHDQGSBBOR-IOVATXLUSA-N	135191	C1[C@H]([C@@H]([C@H](C(O)O)O)O)O	0.16	1.2	135191	11	-1.454	Pentoses	a 1
xylonolactone NIST	XXBSUZSONOQQGK-FLRLBIABSA-N	439692	C1[C@H]([C@@H]([C@H](C(=O)O1)C	1	1.2	439692	16	-0.96	Dicarboxylic Acids	1
xylitol	HEBKCHPVOIAQTA-NGQZQWQHPSA-N	6912	C([C@H]([C@H](CO)O)O)O	0.73	0.95	6912	3	-3.224	Sugar Alcohols	1
xanthine	LRFVITYWQMYALW-UHFFFAOYSA-N	1188	C1=NC2=C(N1)C(=O)NC(=O)N2	0.16	1.1	1188	7	-0.654	Purinones	1
valine	KZSNJWFQEVHDMF-BYPYUCNSA-N	6287	CC(C)[C@@H](C(=O)O)N	0.094	1.4	6287	15	-2.169	Amino Acids, Branched-C	1
uridine	DRTQHJPMVMBUCF-XVFCMESISA-N	6029	C1=CN(C(=O)NC1=O)[C@H]2[C@H	0.86	0.84	6029	9	-2.117	Pyrimidine Nucleosides	1
uric acid	LEHOTFFKMEONL-UHFFFAOYSA-N	1175	C12=C(NC(=O)N1)NC(=O)NC2=O	0.55	0.85	1175	7	-1.191	Purinones	1
urea	XSQKJJFZCRKT-UHFFFAOYSA-N	1176	C(=O)(N)N	0.16	0.65	1176	35	-1.686	Organic Chemicals	1
uracil	ISAKRJGDUQUOIC-UHFFFAOYSA-N	1174	C1=CNC(=O)NC1=O	0.04	1.2	1174	7	-0.875	Pyrimidinones	1
UDP-N-acetylglucosamine	LFTYTUAZOPRMMI-CFRASDGPASA-N	445675	CC(=O)N[C@@H]1[C@@H]([C@@H]([C	0.6	0.83	445675	9	-5.903	Uridine Diphosphate Sug	1
tyrosine	OUYCCASQSFE-MQMMMGPOBSA-N	6057	C1=CC(=CC=C1C[C@@H](C(=O)O)N)	0.0078	1.6	6057	28	-2.711	Amino Acids, Aromatic	1
tryptophan	QIVBCDIJAI PQS-VIFPVBCQESA-N	6305	C1=CC=C2C(=C1)C(=CN2)C[C@@H](C	1	1	6305	10	-2.023	Amino Acids, Aromatic	1
tocopherol alpha-	NCYCYZNXIZOKI-OVSJKPMPASA-N	638015	CC1=C(C(CCC1)(C)C)/C=C/C(=C/C/C/	0.34	0.8	638015	49	6.335	Retinoids	1
thymidine	IQFYKMMVGFJEH-XLPZGREQSA-N	5789	CC1=CN(C(=O)NC1=O)[C@H]2[C@H	0.44	1.1	5789	9	-1.335	Pyrimidine Nucleosides	1
threonine	AYFVYJQAPQTC-CGBXJSLDSA-N	6288	C[C@H]([C@@H](C(=O)O)N)O	0.93	1.1	6288	27	-3.496	Amino Acids	1
terephthalic acid	KKEYFWRCBNT PAC-UHFFFAOYSA-N	7489	C1=CC(=CC=C1C(=O)O)C(=O)O	0.63	1.1	7489	8	-0.118	Phthalic Acids	1
taurine	XOAAWQZATWQOTB-UHFFFAOYSA-N	1123	C(CS(=O)(=O)O)N	0.93	0.7	1123	34	-1.678	Alkanesulfonic Acids	1
succinic acid	KDYFGRWQOYBRFD-UHFFFAOYSA-N	1110	C(C(=O)O)C(=O)O	0.39	0.85	1110	29	-0.71	Dicarboxylic Acids	1
stearic acid	QIQXTHQIDYTRFH-UHFFFAOYSA-N	5281	CCCCCCCCCCCCCCCC(=O)O	0.22	1.2	5281	1	8.708	Saturated FA	b 1
squalene	YYGNTYWPWHGJRM-AAJYLU CBSA-N	638072	CC(=CCC/C(=C)CC/C(=C)CC/C=C/CC/	0.04	0.66	638072	49	11.482	Polyenes	1
spermine	PFNFQXMRSDOHW-UHFFFAOYSA-N	1103	C(CNCCCN)CNCCCN	0.8	1.1	1103	33	-0.682	Spermidine	1
sorbitol	FBPFTZCFMRRESA-JGWLITMVSA-N	5780	C([C@H]([C@H]([C@@H]([C@H]([C@H]	0.44	1.4	5780	21	-3.896	Sugar Alcohols	1
serine	MTCFGRXMLQNBG-REOHLBHASA-N	5951	C([C@@H](C(=O)O)N)O	0.86	1.1	5951	27	-3.956	Amino Acids	1
salicylaldehyde	SMQUZDBALVYZAC-UHFFFAOYSA-N	6998	C1=CC=C(C=C1)C=O	0.011	1.9	6998	8	0.989	Aldehydes	1
ribulose-5-phosphate	FNZLKVNUWIHPS-UHNVVZDZSA-N	439184	C([C@H]([C@H](C(=O)O)O)OP(=C	0.14	1.2	439184	14	-4.396	Ribulosephosphates	1
ribose-5-phosphate	KTPVXOYAKDPRHY-SOOFDHNKSA-N	439167	C([C@@H]1[C@H]([C@H](C(O)O)O)O	0.22	1.4	439167	22	-3.112	Hexosephosphates	1
ribose	HMFHBZSHGGEWLO-SOOFDHNKSA-N	5779	C([C@@H]1[C@H]([C@H](C(O)O)O)O	0.019	1.5	5779	42	-1.454	Pentoses	1
ribonic acid	QXKAIJAYHKRRA-BXZVTAOSA-N	5460677	C([C@H]([C@H]([C@H](C(=O)O)O)O)O	0.39	1.4	5460677	16	-3.067	Dicarboxylic Acids	1
ribitol	HEBKCHPVOIAQTA-ZXFHETKHASA-N	827	C(C(C(C(CO)O)O)O)O	0.67	0.56	827	3	-3.224	Sugar Alcohols	1
pyruvic acid	LCTONWCANYUPLM-UHFFFAOYSA-N	1060	CC(=O)C(=O)O	1	1.1	1060	18	-0.426	Pyruvates	1
pyrophosphate	XPPKVPWQALFU-UHFFFAOYSA-N	1023	OP(=O)(O)OP(=O)(O)O	0.077	0.61	1023	26	-3.476	Diphosphonates	1
putrescine	KIDHWZJUCRJVML-UHFFFAOYSA-N	1045	C(CCN)CN	0.11	0.44	1045	33	-0.626	Biogenic Polyamines	1
p-tolyl glucuronide	JPAUCQAJHLSMQW-XPORZQOISA-N	154035	CC1=CC=C(C=C1)O[C@H]2[C@@H]([	0.39	0.61	154035	19	0.189	Phenols	1
pseudo uridine	PTJWJQPHWPNBW-GBNDHIKLSA-N	15047	C1=C(C(=O)NC(=O)N1)[C@H]2[C@@	0.22	0.63	15047	9	-2.477	Pyrimidine Nucleosides	1
propane-1,3-diol NIST	YPFDHNVDELHUC-UHFFFAOYSA-N	10442	C(CO)CO	0.44	1.4	10442	30	-0.85	Propylene Glycols	1
pimelic acid	WLJVNTCWHIRURA-UHFFFAOYSA-N	385	C(CCC(=O)O)CCC(=O)O	0.44	0.83	385	1	0.575	Dicarboxylic Acids	b 1
phosphoethanolamine	SUH00TKUPISOBE-UHFFFAOYSA-N	1015	C(COP(=O)(O)O)N	0.44	0.79	1015	34	-2.504	Ethanolamines	1
phosphate	NBIIXVUZAF LBC-UHFFFAOYSA-N	1004	OP(=O)(O)O	0.49	0.79	1004	26	-2.247	Polymers	1
phenylalanine	COLNVLDHVWLRIT-QMMMGPBSA-N	6140	C1=CC=C(C=C1)C[C@@H](C(=O)O)N	0.3	1.1	6140	28	-1.575	Amino Acids, Aromatic	1
phenaceturic acid	UTYVDVLMYQPLQB-UHFFFAOYSA-N	68144	C1=CC=C(C=C1)CC(=O)NCC(=O)O	0.86	0.83	68144	28	0.425	Dipeptides	1
pentadecanoic acid	WQEP L UGLDZJY-UHFFFAOYSA-N	13849	CCCCCCCCCCCCCCC(=O)O	0.49	1.3	13849	1	7.001	Saturated FA	b 1
pelargonic acid	FBUKVVPVMBHYJY-UHFFFAOYSA-N	8158	CCCCCCCC(=O)O	0.14	1.3	8158	1	3.587	Saturated FA	b 1
parabanic acid NIST	ZFLIKDUSDBGUC-UHFFFAOYSA-N	67126	C1(=O)C(=O)NC(=O)N1	1	0.97	67126	48	-0.58	Hydantoins	1
pantothenic acid	GHOKWGTUZEAEQD-ZETCQMYHSA-N	6613	CC(C)(CO)[C@H](C(=O)NCCC(=O)O)O	0.093	0.58	6613	47	-1.343	beta-Alanine	1
palmitoleic acid	SECPZKBENQXJG-FPLPWBNLASA-N	445638	CCCCC/C=C\CCCCCCCC(=O)O	0.66	1.6	445638	12	7.054	UnSaturated FA	1
palmitic acid	IPCSVZSSVZVIGE-UHFFFAOYSA-N	985	CCCCCCCCCCCCCCCC(=O)O	0.19	1.1	985	1	7.57	Saturated FA	b 1
palatinitol	SERLAGPUMNYUCK-DCUALPFSSA-N	88735	C([C@@H]1[C@H]([C@@H]([C@@H]([	0.86	0.97	88735	5	-5.004	Disaccharides	1
oxoproline	ODHCTKXNWHHXC-VKHMVHEASA-N	7405	C1CC(=O)N[C@@H]1C(=O)O	0.6	1.2	7405	46	-0.827	Pyrrrolidinones	1
oxalic acid	MUBZPKHOEPUJKR-UHFFFAOYSA-N	971	C(=O)(C=O)O	0.8	1.2	971	18	-0.688	Dicarboxylic Acids	1
ornithine	AHLPHDHMVZTML-BYPYUCNSA-N	6262	C(C[C@@H](C(=O)O)N)CN	0.16	1.4	6262	17	-3.307	Amino Acids, Basic	1
oleic acid	ZQPPMHVWECSIRJ-KTKRTIGZSA-N	445639	CCCCCCCC=C\CCCCCCCC(=O)O	0.34	1.2	445639	12	8.192	UnSaturated FA	1
oleamide NIST	FATBGEAMYMYZAF-KTKRTIGZSA-N	5283387	CCCCCCC/C=C\CCCCCCC(=O)N	1	1.1	5283387	50	7.464	Oleic Acids	1
octanol NIST	KBFLHHGFOOTCA-UHFFFAOYSA-N	957	CCCCCCCCO	0.86	0.74	957	36	3.127	Fatty Alcohols	1
octadecanol	GLDOVTGHNKAZLK-UHFFFAOYSA-N	8221	CCCCCCCCCCCCCCCCCO	0.8	1	8221	37	8.817	Fatty Alcohols	1
noradrenaline	SFLSHLFXELFNJZ-QMMMGPBSA-N	439260	C1=CC(=C(C=C1[C@H](CN)O)O)O	0.55	1.2	439260	19	-0.446	Catecholamines	1
nicotinamide	DFPAKSUCGFBDF-UHFFFAOYSA-N	936	C1=CC(=CN=C1)C(=O)N	0.44	0.76	936	10	-1.236	Nicotinic Acids	1
n-acetyl-d-hexosamine	OVRNDRQMDRJT HS-FMDGEEDCSA-N	24139	CC(=O)N[C@@H]1[C@H]([C@@H]([C	0.16	0.82	24139	47	-1.488	Glucosamine	1

Compound.Name	InChiKeys	Pubchem.ID	SMILES	pvalue	foldchange	CID	ClusterNumber	xlogp	ClusterLabel	TreeLabel: FDR
N-acetylaspartic acid	OTCCIMWXFLJLIA-BYPYZUCNSA-N	65065	CC(=O)N[C@@H](CC(=O)O)C(=O)O	0.49	1.1	65065	31	-1.265	Amino Acids, Acidic	1
myristic acid	TUNFSRHWTWDNC-UHFFFAOYSA-N	11005	CCCCCCCCCCCC(=O)O	1	1.1	11005	1	6.432	Saturated FA	b 1
methylmalonic acid	ZIYVHBGGAAOTLY-UHFFFAOYSA-N	487	CC(C(=O)O)C(=O)O	0.11	1.2	487	29	-0.085	Dicarboxylic Acids	1
methionine sulfoxide	QEFRNWVLZKMPFJ-YGVKFDHGSA-N	158980	CS(=O)CC[C@@H](C(=O)O)N	0.55	1	158980	25	-3.882	Amino Acids, Sulfur	1
methionine	FFEARJCKVFRZR-BYPYZUCNSA-N	6137	CSCC[C@@H](C(=O)O)N	0.16	1.5	6137	25	-1.853	Amino Acids, Sulfur	1
methanolphosphate	CAALPUQFIOTL-UHFFFAOYSA-N	13130	COP(=O)O	1	1.1	13130	26	-1.728	Organophosphates	1
mannose	WQZGKKKJFFOK-QTVWNMPRSA-N	18950	C([C@@H]1[C@H]([C@@H]([C@H]1O)O)O)O	0.16	0.4	18950	4	-1.697	Hexoses	1
mannitol	FBPFTZCFMRRESA-KVTDHHDQSA-N	6251	C([C@H]([C@H]([C@H]([C@H]1O)O)O)O)O	0.39	0.74	6251	21	-3.896	Sugar Alcohols	1
maltotriose	FYGDMLNLYKFZSV-DZOUCCMHSA-N	439586	C([C@@H]1[C@H]([C@@H]([C@H]1O)O)O)O	0.96	1	439586	5	-5.629	Trisaccharides	1
maltose	GUBGYTABKSRVRQ-PICCSMPSSA-N	439186	C([C@@H]1[C@H]([C@@H]([C@H]1O)O)O)O	0.019	0.73	439186	5	-3.663	Disaccharides	1
malic acid	BJEPYKPYRNKOW-UHFFFAOYSA-N	525	C(C(C(=O)O)O)C(=O)O	0.8	1.1	525	2	-1.474	Dicarboxylic Acids	1
lyxose	SRBFZHDQGSBBOR-AGQMPKLSLA-N	439240	C1[C@H]([C@@H]([C@@H]([C@H]1O)O)O)O	1	1	439240	11	-1.454	Pentoses	a 1
lyxitol	HEBKCHPVOIAQTA-IMJISDKUSA-N	439255	C([C@@H]([C@@H]([C@@H]([C@@H]1O)O)O)O)O	0.6	0.47	439255	3	-3.224	Sugar Alcohols	1
lysine	KDXKERNBSIXSRK-YFKPBYRVSA-N	5962	C(CCN)C[C@@H](C(=O)O)N	0.14	1.6	5962	17	-2.949	Amino Acids, Basic	1
linoleic acid	OYHQOLUKZRVRURQ-HZJYTRNSA-N	5280450	CCCC/C=C/C/C=C\CCCCCCC(=O)O	0.86	1.1	5280450	12	7.865	UnSaturated FA	1
lignoceric acid	QZZGJVDVWLFDXLK-UHFFFAOYSA-N	11197	CCCCCCCCCCCCCCCCCCCC(=O)O	0.22	1.2	11197	1	12.122	Saturated FA	b 1
levoglucosan	TWNIBLMWSKIRAT-VFUOHLCSA-N	2724705	C1[C@@H]2[C@H]([C@@H]([C@H]1O)O)O2	0.44	0.94	2724705	39	-1.537	Hexoses	1
leucine	ROHFNLRQFUQHCH-YFKPBYRVSA-N	6106	CC(C)C[C@@H](C(=O)O)N	0.34	1.3	6106	40	-1.389	Amino Acids, Branched-C	1
lauric acid	POULHZVOKOAJMA-UHFFFAOYSA-N	3893	CCCCCCCCCCCC(=O)O	0.024	1.3	3893	1	5.294	Saturated FA	b 1
lactulose	JCQLYHFGKRNPE-FCVZTGTOSA-N	11333	C([C@@H]1[C@H]([C@@H]([C@H]1O)O)O)O	0.19	0.88	11333	39	-3.706	Disaccharides	1
lactic acid	JVTAAEKCFNVCJ-UHFFFAOYSA-N	612	CC(C(=O)O)O	0.86	0.98	612	18	-0.591	Lactates	1
isothreonic acid	JPIQOTBSSVTP-GBXJSLDSA-N	151152	C([C@@H]([C@@H]([C@@H]([C@@H]1O)O)O)O)O	0.3	0.84	151152	2	-2.395	Butyrates	1
isothreitol	UNXHWFMMPAWPVI-QVWZVWQMSA-N	169019	C([C@H]([C@@H]([C@@H]([C@@H]1O)O)O)O)O	0.26	1.2	169019	3	-2.552	Sugar Alcohols	1
isoribose	SRBFZHDQGSBBOR-SOOFDHNKSA-N	10975657	C1[C@H]([C@@H]([C@@H]([C@@H]1O)O)O)O	0.14	1.3	10975657	11	-1.454	Pentoses	a 1
isoleucine	AGPKZVTJJNIPAG-WHFBIKZSA-N	6306	CC[C@H](C)[C@@H](C(=O)O)N	0.077	1.3	6306	40	-1.6	Amino Acids, Branched-C	1
isocitric acid	ODBLHEXUDAPZAU-ZAFYKAAXSA-N	5318532	C([C@@H]([C@@H]([C@@H]([C@@H]1O)O)O)O)O	0.0012	0.22	5318532	43	-2.064	Tricarboxylic Acids	0.21
inositol-4-monophosphate	INAPMGSXUVUWAF-GFWFORPUSA-N	440043	[C@H]1([C@@H]([C@@H]([C@@H]([C@@H]1O)O)O)O)O	0.014	1.4	440043	23	-3.545	Inositol Phosphates	1
inosine 5'-monophosphate	GRSZFWQUAKGDAV-KQYNXXCUSA-N	8582	C1=NC(=O)C2=C(N1)N(C=N2)[C@H]3	1	0.82	8582	6	-2.291	Purine Nucleosides	1
inosine	UGQMVRVMYASFK-QKYNXXCUSA-N	6021	C1=NC(=O)C2=C(N1)N(C=N2)[C@H]3	0.024	0.68	6021	6	-0.633	Purine Nucleosides	1
indoxyl sulfate	BXFFHSIDQOFMLE-UHFFFAOYSA-N	10258	C1=CC=C2C(=C1)C(=CN2)OS(=O)(=O)O	0.3	0.74	10258	10	-0.075	Indoles	1
hypoxanthine	FDGQSTZJBFJUBT-UHFFFAOYSA-N	790	C1=NC2=C(N1)C(=O)N=CN2	0.19	1.2	790	7	0.556	Purinones	1
hydroxylamine	AVXURJPOCDRRFD-UHFFFAOYSA-N	787	NO	0.39	1.5	787	35	-1.604		1
hydroxycarbamate NIST	DRAJWRKLRBNJRQ-UHFFFAOYSA-M	16639161	C(=O)NO	0.26	0.86	16639161	35	-0.878		1
histidine	HNDVDQJICGZPNO-YFKPBYRVSA-N	6274	C1=C(NC(=N1)C[C@@H](C(=O)O)N)N	0.077	1.9	6274	6	-3.429	Amino Acids, Cyclic	1
hexose-6-phosphate	NBSCHQZLSJFNQ-UHFFFAOYSA-N	208	C(C1C(C(C(C(O1)O)O)O)O)OP(=O)(O)O	0.67	1.3	208	13	-3.355	Hexosephosphates	1
hexitol	FBPFTZCFMRRESA-UHFFFAOYSA-N	453	C(C(C(C(C(CO)O)O)O)O)O	0.22	0.71	453	21	-3.896	Sugar Alcohols	1
heptadecanoic acid	KEMQGRYUADPNZ-UHFFFAOYSA-N	10465	CCCCCCCCCCCCCCCC(=O)O	0.26	1.3	10465	1	8.139	Saturated FA	b 1
guanosine	NYHBQMYGNKIUIF-UUOKFMHZA-N	6802	C1=NC2=C(N1[C@H]3[C@@H]([C@@H]3O)O)N	0.019	0.49	6802	6	-0.958	Purine Nucleosides	1
glycolic acid	AEMRFAOFKBGASW-UHFFFAOYSA-N	757	C(C(=O)O)O	0.35	1.5	757	18	-1.117	Glycolates	1
glycocyanine	BPMFZUMJYQTVII-UHFFFAOYSA-N	763	C(C(=O)O)N=C(N)N	0.44	1.2	763	32	-3.974		1
glycine	DHMQDGOQFOQNFH-UHFFFAOYSA-N	750	C(C(=O)O)N	0.11	0.71	750	32	-3.35	Amino Acids	1
glycerol-alpha-phosphate	AWUCVROLDVIAJ-UHFFFAOYSA-N	754	C(COP(=O)(O)O)O	0.019	0.48	754	14	-3.109	Glycerophosphates	1
glycerol	PEDCQBHIVMGVHV-UHFFFAOYSA-N	753	C(C(CO)O)O	0.26	0.68	753	30	-1.88	Sugar Alcohols	1
glyceric acid	RBNPOMFGQQGHHO-UWTATZPHSA-N	439194	C([C@H](C(=O)O)O)O	0.094	2.2	439194	2	-1.723	Sugar Acids	1
glutamine	ZDXPYRPNDDTMRX-VKHMHEASA-N	5961	C(CC(=O)N)[C@@H](C(=O)O)N	0.44	1.3	5961	17	-4.077	Amino Acids, Basic	1
glutamic acid	WHUUTDBJXRKMK-VKHMHEASA-N	33032	CC(C(=O)O)[C@@H](C(=O)O)N	0.86	0.99	33032	17	-3.349	Amino Acids, Acidic	1
glucose-6-phosphate	NBSCHQZLSJFNQ-GASJEMHNSA-N	5958	C([C@@H]1[C@H]([C@@H]([C@H]1O)O)O)O	0.73	1.3	5958	13	-3.355	Hexosephosphates	1
glucose-1-phosphate	HXXFSRBOHSIMQ-VFUOHLCSA-N	65533	C([C@@H]1[C@H]([C@@H]([C@H]1O)O)O)O	0.0012	0.55	65533	13	-3.355	Hexosephosphates	0.21
glucose	WQZGKKKJFFOK-VFUOHLCSA-N	64689	C([C@@H]1[C@H]([C@@H]([C@H]1O)O)O)O	0.34	0.9	64689	4	-1.697	Hexoses	1
gluconic acid	RGHNJXEOKUKBD-QTDBOELSSA-N	6857417	C([C@@H]([C@@H]([C@@H]([C@@H]1O)O)O)O)O	0.89	0.96	6857417	16	-3.739	Sugar Acids	1
galacturonic acid	AEMOLEFTQBMLNQ-DTEWJGMSA-N	441476	[C@@H]1([C@@H]([C@@H]([C@@H]1O)O)O)O	0.19	0.52	441476	44	-1.54	Hexuronic Acids	1
galactose-6-phosphate	NBSCHQZLSJFNQ-SVZMEIOVSA-N	439404	C([C@@H]1[C@H]([C@@H]([C@H]1O)O)O)O	0.48	1.4	439404	13	-3.355	Hexosephosphates	1
galactose	WQZGKKKJFFOK-PHYPRBDBSA-N	439357	C([C@@H]1[C@H]([C@@H]([C@H]1O)O)O)O	0.8	1.1	439357	4	-1.697	Hexoses	1
galactinol	VCWWRQDBPZXKXG-ZNVDFQESA-N	11727586	C([C@@H]1[C@H]([C@@H]([C@H]1O)O)O)O	0.3	1.2	11727586	5	-3.424	Disaccharides	1
fumaric acid	VZCYOQTPCHFL-OWOJBTEDSA-N	444972	C=C/C(=O)O\C(=O)O	0.73	1.1	444972	20	-0.416	Dicarboxylic Acids	1
fucose	SHZGJCMBGCMKK-FPRJBLGDSA-N	439650	C([C@@H]1[C@H]([C@@H]([C@@H]1O)O)O)O	0.67	1	439650	4	-0.994	Hexoses	1
fructose-6-phosphate	BGWGXPPYQGQALX-ARQDHWQXSA-N	440641	C([C@@H]1[C@H]([C@@H]([C@@H]1O)O)O)O	0.49	1.6	440641	22	-3.398	Hexosephosphates	1
fructose-1-phosphate	RHKKZBWRNHGJZ-VRPWFDPXSA-N	439394	C([C@@H]1[C@H]([C@@H]([C@@H]1O)O)O)O	0.0028	1.8	439394	22	-3.398	Hexosephosphates	0.47
fructose	RFSUNEUAIZKAJO-ARQDHWQXSA-N	439709	C([C@@H]1[C@H]([C@@H]([C@@H]1O)O)O)O	0.3	1.4	439709	42	-1.74	Hexoses	1

Compound.Name	InChiKeys	Pubchem.ID	SMILES	pvalue	foldchange	CID	ClusterNumber	xlogp	ClusterLabel	TreeLabel:FDR
ethanolamine	HZAXFHJVLSVMW-UHFFFAOYSA-N	700	C(CO)N	0.6	0.95	700	34	-1.275	Ethanolamines	1
erythronic acid lactone	SGMJBNSHAZVGMC-PWNYCUMCSA-N	5325915	C1[C@H]([C@H]([C@H](C=O)O1)O)O	0.35	0.97	5325915	2	-0.717	Butyrates	1
epsilon-caprolactam	JBKVHLHDHXXEQ-UHFFFAOYSA-N	7768	C1CCC(=O)NCC1	0.44	1.6	7768	50	0.404	Lactams	1
enolpyruvate NIST	DTBNBXWJWCWKI-UHFFFAOYSA-N	1005	C=C(C(=O)O)OP(=O)(O)O	0.55	1.2	1005	20	-1.296	Hydroxy Acids	1
dodecanol	LQZZUXJYWNFBMV-UHFFFAOYSA-N	8193	CCCCCCCCCCCO	0.094	1.8	8193	36	5.403	Fatty Alcohols	1
dihydroxyacetone	RXKJFZQQPQGTFL-UHFFFAOYSA-N	670	C(C(=O)O)O	0.39	0.94	670	30	-1.889	Ketoses	1
dihydrocholesterol	QYIXCDOBOSTCEI-FBVYSKEZSA-N	66066	C[C@H]([CCCC(C)C][C@H]1CC[C@@H]1O)O	0.51	1.3	66066	45	11.783	Cholestanes	c 1
deoxycholic acid	KXGVVGMKQFVNSR-LLQZFEFROSA-N	222528	C[C@H]([CCCC(C)C][C@H]1CC[C@@H]1O)O	0.34	0.68	222528	45	5.756	Cholic Acids	c 1
dehydroascorbic acid	SBJKFFYZUCET-JLAZNSOCSA-N	440667	C([C@@H]([C@@H]1C(=O)C(=O)C(=O)O1)O)O	0.19	0.74	440667	44	-1.878	Sugar Acids	1
dehydroabiatic acid	NFWKVVVWBFBAOV-MISYRCLQSA-N	94391	CC(C)C1=CC=C(C=C1)[C@H]3[C@@H](C)CC[C@H]3O	0.86	1.2	94391	8	5.656	Diterpenes, Abietane	1
cytidine-5-monophosphate	IERHLVCPMICTF-XVFCMESISA-N	6131	C1=CN(C(=O)N=C1N)[C@H]2[C@@H](NC(=O)N)C(=O)N2	0.11	0.093	6131	9	-3.851	Cytosine Nucleotides	1
cysteine	XUJNEKLAYXESH-REOHLBHSA-N	5862	C([C@@H]([C@@H](O)N)S)C(=O)O	0.077	2.4	5862	25	-2.575	Amino Acids, Sulfur	1
cyclohexylamine	PAFZNLMFXTMII-UHFFFAOYSA-N	7965	C1CCC(CC1)N	0.14	1.6	7965	33	1.262	Cycloparaffins	1
creatinine	DDRJAANPRJIHG-UHFFFAOYSA-N	588	CN1CC(=O)N=C1N	0.6	0.67	588	48	-0.126	Imidazoles	1
conduritol-beta-epoxide	ZHMWVQGCZINIHW-SPHYCDKFSAN	9989541	[C@H]1[C@@H]([C@H]2C[C@@H]1O)O2	0.064	1.7	9989541	23	-1.727	Cycloparaffins	1
citrulline	RHGKLRLOHDJDR-BYPYUCNSA-N	9750	C(C[C@@H](C(=O)O)N)CNC(=O)N	0.3	1.4	9750	46	-3.909	Amino Acids	1
citric acid	KRKNYBCHXYNGOX-UHFFFAOYSA-N	311	C(C(=O)O)(CC(=O)O)(C(=O)O)O	0.00029	0.099	311	43	-2.247	Tricarboxylic Acids	0.05
cholesterol	HVVYWMOMLDIMFJA-DPAQBDFISA-N	5997	C[C@H]([CCCC(C)C][C@H]1CC[C@@H]1O)O	0.26	0.84	5997	38	10.518	Cholestanes	1
cellobiose	GUBGYTABKSRVRQ-QUYVBRFLSA-N	6255	C([C@@H]1[C@H]([C@@H]([C@H]([C@@H](O1)O)O)O)O)O	0.094	0.56	6255	5	-3.663	Disaccharides	1
capric acid	GHNVFZFCNZKVT-UHFFFAOYSA-N	2969	CCCCCCCCC(=O)O	0.024	1.4	2969	1	4.156	Saturated FA	b 1
beta-sitosterol	KJWDPNRRJALLNS-VJFFXLSFSA-N	222284	CC[C@H]([CC]([C@@H]([C@H]1CC[C@@H]1O)O)O)O	0.34	0.78	222284	38	11.959	Cholestanes	1
beta-glycerolphosphate	DHCLVCXQBOPH-UHFFFAOYSA-N	2526	C(C(=O)OP(=O)(O)O)O	0.26	0.84	2526	14	-3.109	Glycerophosphates	1
beta-alanine	UCMIRNVEIXFBKS-UHFFFAOYSA-N	239	C(CN)C(=O)O	0.73	1.2	239	41	-1.026	Amino Acids	1
benzylalcohol	WVDDGKGMKODPV-UHFFFAOYSA-N	2879	CC1=CC=C(C=C1)O	0.16	1.5	2879	19	1.338	Phenols	1
benzoic acid	WPYMKLBDIGXBTP-UHFFFAOYSA-N	243	C1=CC=C(C=C1)O=O	0.44	1.7	243	8	0.982	Benzoates	1
aspartic acid	CKLJMWZTZICHS-REOHLBHSAN	5960	C([C@@H]([C@@H]([C@@H](C(=O)O)N)C(=O)O)O)O	0.077	1.4	5960	31	-3.707	Amino Acids, Acidic	1
asparagine	DCXYFEDJODNFA-REOHLBHSAN	6267	C([C@@H]([C@@H]([C@@H](C(=O)O)N)C(=O)O)O)O	0.26	1.2	6267	31	-4.435	Amino Acids, Basic	1
ascorbic acid	CIWBSSHKKDKBK-LJAZNSOCSAN	54670067	C([C@@H]([C@@H]1C(C=C(C(=O)O1)O)O)O)O	0.34	0.43	54670067	20	-0.178	Sugar Acids	1
arachidonic acid	YZKBAPSDXZRG-DOFZRALISA-N	444899	CCCCC/C=C/C/C=C/C/C=C/C/C=C/C/C=C/C/C=C/C/C=C/C	0.26	1	444899	12	8.349	Unsaturated FA	1
arachidic acid	VKOBVWKNKXDXE-UHFFFAOYSA-N	10467	CCCCCCCCCCCCCCCC(=O)O	0.67	1.4	10467	1	9.846	Saturated FA	b 1
arabitol	HEBKHPVOIAQTA-QWVZVWQMSA-N	94154	C([C@H]([C@@H]([C@@H]([C@@H]([C@@H](O)O)O)O)O)O	0.22	0.62	94154	3	-3.224	Sugar Alcohols	1
arabinose	SRBFZHDQGSBBOR-ZRMNMSDTSAN	6902	C1[C@H]([C@@H]([C@H]([C@@H](C1O)O)O)O)O	0.0078	1.6	6902	11	-1.454	Pentoses	a 1
aminomalonic acid	JINBYESILADKFW-UHFFFAOYSA-N	100714	C(C(=O)O)(C(=O)O)N	0.063	0.36	100714	27	-3.523	Dicarboxylic Acids	1
allantoic acid	NUCLJNSWZCHRKL-UHFFFAOYSA-N	203	C(C(=O)O)(NC(=O)N)NC(=O)N	0.45	0.55	203	32	-2.924		1
alanine	QNAVYBMKLOCPYG-REOHLBHSAN	5950	C[C@H]([C@@H](O)N)C(=O)O	0.86	0.81	5950	15	-2.824	Amino Acids	1
adenosine-5-monophosphate	UDMBCSSLTHHNC-QKYNXXCUSA-N	6083	C1=NC2=C(C(=N1)N)N=CN2[C@H]3[C@H]([C@@H]([C@@H]([C@@H]([C@@H]3O)O)O)O)O	0.39	0.63	6083	24	-4.025	Purine Nucleosides	1
adenosine	OIRDTQYFTABQQC-KQYNXXCUSA-N	60961	C1=NC2=C(C(=N1)N)N=CN2[C@H]3[C@H]([C@@H]([C@@H]([C@@H]3O)O)O)O	0.44	0.88	60961	24	-2.367	Purine Nucleosides	1
adenine	GFFGJXGJBIJGV-UHFFFAOYSA-N	190	C1=NC2=C(N1)C(=NC=N2)N	0.077	0.71	190	7	-1.287	Purines	1
aconitic acid	GTZCVFVGUGFEME-IWQZHSRSA-N	643757	C/C=C(C(=O)O)/C(=O)O	0.00029	0.39	643757	20	-1.034	Tricarboxylic Acids	0.05
acetophenone NIST	KWOLFJPFCHCOG-UHFFFAOYSA-N	7410	CC(=O)C1=CC=CC=C1	0.44	1.3	7410	8	1.244	Acetophenones	1
5-methoxytryptamine	JTEJPPKMYBDEMY-UHFFFAOYSA-N	1833	COC1=CC=C(C=C1)NC(=O)C2=CC=CC=C2	1	1.4	1833	10	0.687	Serotonin	1
5-hydroxy-3-indoleacetic acid	DUUGKQCCEGLZNO-UHFFFAOYSA-N	1826	C1=CC2=C(C=C1O)C(=CN2)CC(=O)O	0.14	1.2	1826	10	0.513	Indoleacetic Acids	1
5'-deoxy-5'-methylthioadenosine	WUUGFSXJNOTRMR-IOSLPCCCSA-N	439176	CSC[C@H]1[C@H]([C@H]([C@@H]1O)O)O	0.55	0.87	439176	24	-1.051	Purine Nucleosides	1
4-hydroxybutyric acid	SJZRECIVHDYJC-UHFFFAOYSA-N	10413	C(CC(=O)O)O	1	0.86	10413	29	-0.601	Butyrates	1
3-phosphoglycerate	OSJPPGNTCRNQQC-UHFFFAOYSA-N	724	C(C(C(=O)O)OP(=O)(O)O)O	0.11	1.2	724	14	-2.952	Sugar Acids	1
3-hydroxybutyric acid	WHBMMWSBFZVSSR-GSVOUGTGSAN	92135	C[C@H]([C@@H](O)O)O	0.73	0.87	92135	2	-0.499	Butyrates	1
3-aminoisobutyric acid	QCHPKSFMDFHSPNR-UHFFFAOYSA-N	64956	CC(CN)C(=O)O	0.73	0.74	64956	41	-0.733	Amino Acids	1
2-monopalmitin	BBNYCLAREVXOSG-UHFFFAOYSA-N	123409	CCCCCCCCCCCC(=O)OC(CO)CO	0.39	0.64	123409	1	6.51	Glycerides	b 1
2-hydroxypyrazinyl-2-propeno	WVZVBCSNPDDHI-FNORWQNLISA-N	5371086	CCOC(=O)C(=O)/C=C/C1=NC=NC=N1	0.34	1.5	5371086	15	0.649		1
2-hydroxyglutaric acid	HWXBTVAVRSUOIR-UHFFFAOYSA-N	43	C(CC(=O)O)C(C(=O)O)O	0.12	1.6	43	16	-1.116	Dicarboxylic Acids	1
2-aminobutyric acid	QWKQKZIFLGMDS-UHFFFAOYSA-N	6657	CCC(C(=O)O)N	0.22	1.4	6657	15	-2.466	Butyrates	1
2,3-dihydroxybutanoic acid NIST	LOUGYXZSURQALL-UHFFFAOYSA-N	250402	CC(C(C(=O)O)O)O	0.27	1.2	250402	2	-1.263	Sugar Acids	1
1-methylinosine	WJNGQIYELQJMN-IOSLPCCCSA-N	65095	CN1C=NC2=C(C1=O)N=CN2[C@H]3[C@H]([C@@H]([C@@H]([C@@H]3O)O)O)O	0.6	0.86	65095	6	-1.805	Purine Nucleosides	1
1-hexadecanol	BXWNKGSJHAJOGX-UHFFFAOYSA-N	2682	CCCCCCCCCCCCCCCCO	0.55	0.85	2682	37	7.679	Fatty Alcohols	1
1,5-anhydroglucitol	MPCAJMNYNOGXPB-SLPGGIOYSA-N	64960	C1[C@H]([C@H]([C@@H]([C@H]([C@H]1O)O)O)O)O	0.31	0.6	64960	4	-1.591	Hexoses	1
1,2-anhydro-myoinositol NIST	ZHMWVQGCZINIHW-FTYOSCRSSAN	119054	C([C@H]1[C@@H]([C@H]([C@@H]([C@H]1O)O)O)O)O	0.55	0.79	119054	23	-1.727	Cycloparaffins	1
1,2,4-benzenetriol	GGNQRNBDZQJCCN-UHFFFAOYSA-N	10787	C1=CC(=C(C=C1)O)O	0.11	1.9	10787	19	1.002	Phenols	1

**Table S7. Results of the ChemRICH enrichment analysis for the altered metabolites in Zn-deficient vs Zn-sufficient middle-aged rat prostates (Wistar-Unilever strain)**

Cluster name	Cluster size	p-values	FDR	Key compound	Altered metabolites	Increased	Decreased
Tricarboxylic Acids	3	0.0025	0.06	citric acid	3	0	3
Pentoses	5	0.0083	0.1	arabinose	2	2	0
Saturated FA	10	0.02	0.16	lauric acid	2	2	0
Hexosephosphates	7	0.27	1	glucose-1-phosphate	2	1	1
Purine Nucleosides	7	0.33	1	guanosine	2	0	2
Amino Acids	7	1	1	glycine	0	0	0
Amino Acids, Acidic	3	1	1	aspartic acid	0	0	0
Amino Acids, Aromatic	3	1	1	tyrosine	1	1	0
Amino Acids, Basic	4	1	1	lysine	0	0	0
Amino Acids, Branched-Chai	3	1	1	isoleucine	0	0	0
Amino Acids, Sulfur	3	1	1	cysteine	0	0	0
Butyrates	5	1	1	2-aminobutyric acid	0	0	0
Cholestanes	3	1	1	cholesterol	0	0	0
Cycloparaffins	3	1	1	conduritol-beta-epoxide	0	0	0
Dicarboxylic Acids	10	1	1	aminomalonnate	0	0	0
Disaccharides	5	1	1	maltose	1	0	1
Fatty Alcohols	4	1	1	dodecanol	0	0	0
Hexoses	7	1	1	mannose	0	0	0
Phenols	3	1	1	1,2,4-benzenetriol	0	0	0
Purinones	3	1	1	xanthine	0	0	0
Pyrimidine Nucleosides	3	1	1	pseudo uridine	0	0	0
Sugar Acids	6	1	1	glyceric acid	0	0	0
Sugar Alcohols	9	1	1	hexitol	0	0	0
UnSaturated FA	4	1	1	arachidonic acid	0	0	0