



**Supplementary Fig. 3** Sensitivity profiles for healthy older subjects. Sensitivity analysis was performed only for the most promising models.

**Supplementary table 1** Correlation matrices for parameters in model #1 sensitivity/specificity analysis

Warm							
Younger subjects				Older subjects			
	$K_1$	$k_2$	$v_b$		$K_1$	$k_2$	$v_b$
$K_1$	1			$K_1$	1		
$k_2$	0.88	1		$k_2$	0.89	1	
$v_b$	-0.27	-0.26	1	$v_b$	-0.38	-0.29	1
Cold							
Younger subjects				Older subjects			
	$K_1$	$k_2$	$v_b$		$K_1$	$k_2$	$v_b$
$K_1$	1			$K_1$	1		
$k_2$	0.87	1		$k_2$	0.86	1	
$v_b$	-0.34	-0.18	1	$v_b$	-0.39	-0.26	1

Initial kinetic parameter values were based on human data (20 younger subjects, 7 older subjects). Strong correlations are highlighted.

**Supplementary table 2** Correlation matrices for parameters in model #4 sensitivity/specificity analysis

Warm									
Younger controls					Older controls				
	$K_1$	$k_2$	$k_3$	$v_b$		$K_1$	$k_2$	$k_3$	$v_b$
$K_1$	1				$K_1$	1			
$k_2$	0.60	1			$k_2$	0.85	1		
$k_3$	-0.75	-0.10	1		$k_3$	-0.50	-0.089	1	
$v_b$	-0.33	-0.17	0.29	1	$v_b$	-0.43	-0.29	0.27	1
Cold									
Younger controls					Older controls				
	$K_1$	$k_2$	$k_3$	$v_b$		$K_1$	$k_2$	$k_3$	$v_b$
$K_1$	1				$K_1$	1			
$k_2$	0.91	1			$k_2$	0.92	1		
$k_3$	0.59	0.84	1		$k_3$	0.65	0.88	1	
$v_b$	-0.44	-0.33	-0.23	1	$v_b$	-0.47	-0.36	-0.23	1

Initial kinetic parameter values were based on human data (20 younger subjects, 7 older subjects). Strong correlations are highlighted.

**Supplementary table 3** Correlation matrices for parameters in model #7 sensitivity/specificity analysis.

Warm									
Younger controls					Older controls				
	$K_1$	$k_2$	$k_3$	$v_b$		$K_1$	$k_2$	$k_3$	$v_b$
$K_1$	1				$K_1$	1			
$k_2$	0.87	1			$k_2$	0.90	1		
$k_3$	-0.82	-0.60	1		$k_3$	-0.98	-0.80	1	
$v_b$	-0.37	-0.34	0.34	1	$v_b$	-0.43	-0.32	0.46	1
Cold									
Younger controls					Older controls				
	$K_1$	$k_2$	$k_3$	$v_b$		$K_1$	$k_2$	$k_3$	$v_b$
$K_1$	1				$K_1$	1			
$k_2$	0.71	1			$k_2$	0.85	1		
$k_3$	-0.62	-0.076	1		$k_3$	0.39	0.79	1	
$v_b$	-0.37	-0.18	0.098	1	$v_b$	-0.45	-0.31	-0.12	1

Initial kinetic parameter values were based on human data (20 younger subjects, 7 older subjects). Strong correlations are highlighted.

**Supplementary table 4** Correlation matrices for parameters in model #10  
sensitivity/specificity analysis

Warm													
Younger controls							Older controls						
	$K_1$	$k_2$	$k_3$	$k_4$	$k_5$	$v_b$		$K_1$	$k_2$	$k_3$	$k_4$	$k_5$	$v_b$
$K_1$	1						$K_1$	1					
$k_2$	0.94	1					$k_2$	0.95	1				
$k_3$	0.73	0.91	1				$k_3$	0.83	0.94	1			
$k_4$	0.83	0.80	0.61	1			$k_4$	0.79	0.81	0.65	1		
$k_5$	0.046	0.051	0.028	0.26	1		$k_5$	0.99	0.94	0.82	0.77	1	
$v_b$	-0.50	-0.44	-0.29	-0.37	-0.004	1	$v_b$	-0.31	-0.23	-0.17	-0.19	-0.32	1
Cold													
Younger controls							Older controls						
	$K_1$	$k_2$	$k_3$	$k_4$	$k_5$	$v_b$		$K_1$	$k_2$	$k_3$	$k_4$	$k_5$	$v_b$
$K_1$	1						$K_1$	1					
$k_2$	0.10	1					$k_2$	0.066	1				
$k_3$	0.88	-0.2	1				$k_3$	-0.073	-1	1			
$k_4$	0.95	0.23	0.77	1			$k_4$	-0.98	0.071	-0.058	1		
$k_5$	0.83	-0.43	0.97	0.72	1		$k_5$	-0.35	-0.96	0.96	0.22	1	
$v_b$	-0.057	-0.38	0.15	-0.12	0.20	1	$v_b$	0.10	0.29	-0.31	-0.11	-0.33	1

Initial kinetic parameter values were based on human data (20 younger subjects, 7 older subjects). Strong correlations are highlighted.