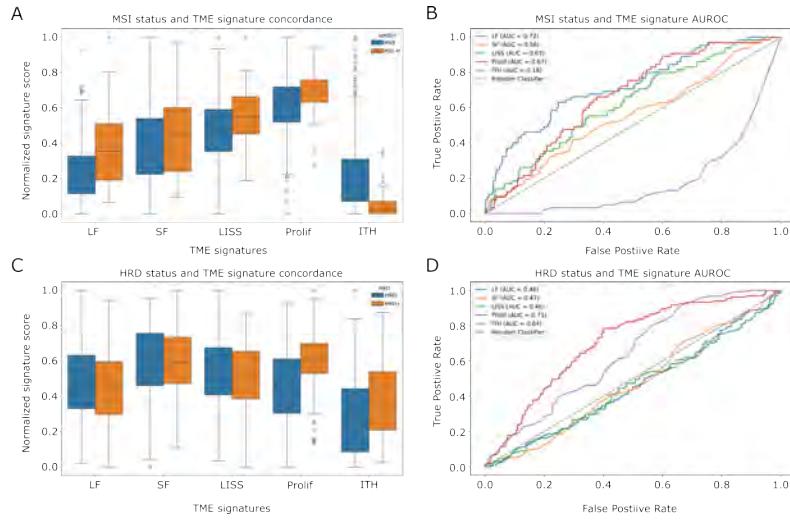
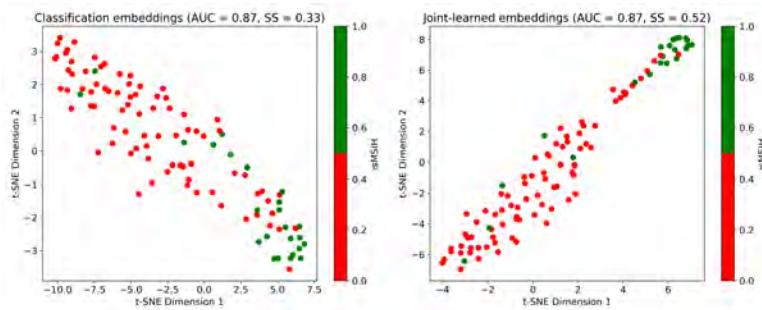


A Supplementary material



Suppl. Fig. 1. The relationship between TME signatures, and **a,b** MSI and **c,d** HRD.



Suppl. Fig. 2. Visualization of the classification and joint-learned embeddings for MSI of the external cohort (n=105) using t-SNE

Suppl. Table 1. Performance overview of weakly-supervised MSI prediction models with 95% confidence intervals.

	TCGA-CRC MSI		CPTAC-CRC MSI	
	AUC	PRC	AUC	PRC
SOTA	70.0 [-]	-	82.0 [-]	-
baseline	86.1 [76-92]	61.4 [46-81]	86.4 [81-91]	70.5 [52-77]
naive	86.4 [79-93]	62.7 [46-82]	88.2 [85-92]	72.4 [67-78]
dwa	84.2 [78-89]	58.7 [47-75]	87.7 [83-93]	70.8 [61-79]
uncert	86.0 [77-92]	63.4 [49-81]	88.4 [85-92]	72.6 [62-79]
autol	94.0 [86-99]	84.5 [70-96]	86.9 [81-91]	73.1 [66-78]
graddrop	85.8 [78-92]	61.2 [48-79]	87.3 [82-92]	71.7 [61-78]
pcgrad	85.4 [78-90]	62.4 [50-79]	87.3 [83-91]	72.0 [62-80]
cagrad	86.5 [78-92]	62.7 [45-83]	89.7 [87-92]	76.6 [71-81]
dwa + graddrop	85.5 [79-92]	59.8 [45-79]	87.6 [84-92]	71.6 [59-80]
dwa + pcgrad	85.6 [79-91]	62.3 [50-81]	88.8 [86-92]	73.3 [64-80]
dwa + cagrad	85.8 [79-91]	59.9 [46-79]	88.4 [84-91]	73.8 [68-78]
uncert + graddrop	85.5 [79-92]	60.7 [47-79]	87.6 [84-92]	71.7 [61-79]
uncert + pcgrad	86.7 [81-91]	62.5 [50-78]	89.0 [86-93]	74.2 [65-81]
uncert + cagrad	86.3 [79-92]	60.7 [47-80]	88.9 [86-92]	74.6 [66-80]
autol + graddrop	85.3 [77-93]	61.6 [45-82]	86.7 [81-91]	69.4 [59-79]
autol + pcgrad	86.1 [78-93]	63.2 [48-81]	87.9 [83-92]	73.6 [67-79]
autol + cagrad	86.5 [78-92]	62.0 [47-82]	89.9 [87-93]	76.3 [72-80]

Suppl. Table 2. Performance overview of weakly-supervised HRD biomarker prediction models with 95% confidence intervals.

	TCGA-LUAD HRD		CPTAC-LUAD HRD	
	AUC	PRC	AUC	PRC
SOTA	70.0 [65-75]	-	82.0 [78-86]	-
baseline	71.6 [64-77]	57.7 [49-65]	81.0 [72-86]	30.3 [25-40]
naive	69.6 [56-79]	57.6 [48-69]	81.2 [74-87]	33.7 [27-42]
dwa	73.3 [67-79]	60.3 [53-66]	83.6 [76-89]	40.8 [28-53]
uncert	73.2 [68-79]	60.1 [52-66]	83.1 [74-88]	41.5 [29-50]
autol	72.2 [63-78]	58.5 [49-67]	85.2 [84-87]	43.0 [37-48]
graddrop	71.1 [64-79]	58.8 [51-67]	84.4 [80-88]	42.5 [33-51]
pcgrad	72.1 [65-80]	60.4 [51-69]	84.1 [80-87]	41.2 [30-49]
cagrad	72.6 [62-79]	58.7 [48-66]	85.4 [81-89]	42.1 [39-46]
dwa + graddrop	72.6 [66-79]	58.4 [51-65]	83.3 [77-88]	40.2 [30-50]
dwa + pcgrad	73.4 [67-81]	59.8 [51-67]	83.0 [77-87]	39.1 [28-49]
dwa + cagrad	71.8 [62-79]	57.9 [47-68]	85.5 [83-88]	44.3 [41-48]
uncert + graddrop	72.6 [66-79]	59.4 [52-65]	83.9 [78-89]	42.3 [31-53]
uncert + pcgrad	71.8 [63-81]	55.4 [50-68]	83.6 [80-87]	39.9 [30-49]
uncert + cagrad	72.4 [64-79]	58.8 [47-67]	84.4 [80-88]	41.9 [35-47]
autol + graddrop	70.8 [63-77]	56.0 [50-64]	84.8 [82-88]	43.4 [36-55]
autol + pcgrad	72.0 [64-78]	58.2 [53-65]	85.6 [83-87]	42.8 [36-52]
autol + cagrad	71.9 [64-77]	57.0 [49-64]	86.1 [84-89]	43.8 [35-54]