APPENDIX S1. NOTATIONS

TABLE S1
SUMMARY OF MATHEMATICAL NOTATIONS AND DESCRIPTIONS USED IN THIS WORK.

Symbol	Description	Symbol	Description
X	Multimodal input information	h_g	Genomic features
V	Visual input information	W_q, W_o	Learnable weights
G	Genomic input information	P	Causal-confounded input feature
T	Clinical text input information	C	Causal signals
Y	Outcome label	N	Confounding factors
S	Observable contextual covariates	E	Non-causal/non-confounding factors
U	Confounding variables	c_Z	Dominant causal component
U_v	Visual confounding variables	c_E, c_N	Suppressed residual terms
M	Mediator variable	$\mathcal{F}_{\mathbf{M}}(\cdot)$	Filtering function parameterized by M
M_v	Visual mediator variable	Q	Mediator-aligned semantic bottleneck
M_g	Genomic mediator variable	$\mathbf{Z_P}$	Reconstructed causal representation
$I(\cdot)$	Mutual information	$\mathcal{L}_{\text{bag}}$	Bag-level classification loss
NDE	Negligible direct effect	$\mathcal{L}_{\text{inst}}$	Instance-level clustering loss
$\psi(\cdot), g(\cdot)$	Feature mapping functions	$\mathcal{L}_{\text{causal}}$	Causal consistency loss
η_{dir}	A small constant for NDE	$\mathcal{L}_{\text{align}}$	Modal alignment constraint
H	Slide-level patch sequence	$\mathcal{L}_{\text{ent}}$	Entropy regularization term
f_{loc}	Local visual information	$\mathcal{L}_{\text{total}}^{\text{cls}}$	Total classification loss
f_{glb}	Global visual information	$\mathcal{L}_{\text{total}}^{\text{surv}}$	Total survival prediction loss
N_{glb}	Number of global tokens	$\mathbf{s}$	Slide-level logits
h_v	Aggregated visual features	p_{full}	Prediction with deconfounded logic
h_t	Clinical text features	p_{med}	Counterfactual prediction variant
$h_{\text{top/bottom}}$	Top-k / Bottom-k instances	$\lambda_{a,c,e}$	Hyperparameters for regularization

APPENDIX S2. PROOFS OF THEORETICAL RESULTS

S2.1. Proof of Theorem III.7

Proof. (i) By Assumption III.4, the mechanism for Y is written as $Y = g(M_v, M_g, h_t)$. In the ideal scenario, this is equivalent to $Y \perp H \mid (M_v, M_g, h_t)$, thus the natural direct effect is approximately zero:

$$I(Y; H \mid M_v) \leq \eta_{\text{v}} \quad \Longrightarrow \quad \text{NDE}(H \to Y) \approx 0 \tag{28}$$

(ii) Because the mediator variable is constructed as

$$M_v = \psi\left(\mathbf{f}_{loc}, \mathbf{f}_{glb}\right) = \text{LGCA}\left(f_{loc}, f_{glb}\right) = \psi(H) \tag{29}$$

So according to the statement of Assumption III.5: $H \to (f_{\text{loc}}, f_{\text{glb}}) \to M_v$. Under the structural equation semantics, any factor affecting M_v cannot enter $\psi(\cdot)$ without passing through H. Therefore, there exists no backdoor common cause that can affect both H and M_v while bypassing H.

(iii) Since f_{glb} serves as an aggregation of global information, it explicitly encodes the confounding factors U_v inherent in the entire slice. Consequently, according to Assumption III.6, conditioned on f_{glb}, the mediator M_v and the unobserved confounders U_v are rendered mutually independent:

$$U_v \perp M_v \mid f_{glb} \quad \Longrightarrow \quad I(U_v; M_v \mid \mathbf{f_{glb}}) \approx \ 0 \tag{30}$$

□

S2.2. Proof of Corollary III.8

Proof. (i) By Assumption III.4, the mechanism for Y is written as $Y = g(M_v, M_g, h_t)$. In the ideal scenario, this is equivalent to $Y \perp h_g \mid (M_v, M_g, h_t)$, thus the natural direct effect is approximately zero:

$$I(Y; h_g \mid M_g) \leq \eta_{\text{g}} \quad \Longrightarrow \quad \text{NDE}(h_g \to Y) \approx 0 \tag{31}$$

(ii) Because the mediator variable is constructed as

$$M_g = \psi\left(\mathbf{h}_g, \mathbf{f}_{loc}, h_t\right) = \text{CLA}(\text{CLA}(h_g, f_{loc}), h_t) \tag{32}$$

According to Assumption III.5, the gene mediator is constructed as $M_g = \psi(h_g, \cdot)$, yielding the causal link $h_g \to M_g$. Under the structural equation semantics, U_g can affect M_g only through its influence on h_g, since $\psi(\cdot)$ does not admit direct inputs from U_g. Therefore, there is no backdoor path from U_g to M_g that bypasses h_g.

(iii) Let the joint observed context be $\mathcal{Z} = \{h_g, \mathbf{f}_{loc}, h_t\}$ and construct the gene mediator via $M_g = \psi(h_g, \mathbf{f}_{loc}, h_t) = \mathrm{CLA}(\mathrm{CLA}(h_g, \mathbf{f}_{loc}), h_t)$. Since $\psi(\cdot)$ is a deterministic mapping, the structural equation for M_g depends exclusively on $\mathcal{Z}$ and admits no direct input from the unobserved confounder U_g. This implies a causal chain $U_g \to \mathcal{Z} \to M_g$. Consequently, M_g is conditionally independent of U_g given $\mathcal{Z}$:

$$U_g \perp M_g \mid \mathcal{Z} \quad \Longrightarrow \quad I(U_g; M_g \mid \mathcal{Z}) = 0. \tag{33}$$

This confirms that the construction mechanism effectively blocks any backdoor path from U_g to M_g that bypasses the observed context $\mathcal{Z}$.

$$I(U_g; M_g \mid h_g, \mathbf{f}_{loc}, h_t) \approx 0, \tag{34}$$

Consequently, the back-door influence of U_g on the mediator pathway is negligible, completing the proof.

□

S2.3. Theoretical Analysis of Section III-D.2

Proof. The proof proceeds by analyzing the signal propagation through the two-stage LWA module, utilizing the linearity of the attention mechanism and the semantic separability properties defined in Assumption III.9 and Definition III.10.

Definition (LMA). We define the LMA operator as

$$\mathrm{LMA}(\mathbf{a}, \mathbf{b}, \mathbf{c}) = \mathbf{W}_o \left(\mathrm{Softmax}\left(\frac{(\mathbf{W}_q \mathbf{a})\, \mathbf{b}^\top}{\sqrt{D}} \right) \mathbf{c} \right). \tag{35}$$

Stage I (Block confounding factors). In the first attention layer, the mediator dictionary $\mathbf{M}$ queries the input features $\mathbf{P}$ and produces an intermediate representation

$$\mathbf{Q} \;=\; \mathrm{LWA}(\mathbf{M}, \mathbf{P}, \mathbf{P}) \;=\; \mathcal{F}_{\mathbf{M}}(\mathbf{P}) \;=\; \mathbf{c}_Z + \mathbf{c}_E + \mathbf{c}_N, \tag{36}$$

Based on the definition of LMA, it is essentially a scaled dot-product attention mechanism that uses the mediator dictionary $\mathbf{M}$ to compute attention weights and re-aggregate the input feature. Therefore, LWA acts as a *semantic filtering* function: it amplifies mediator-aligned (causal) semantics while attenuating unrelated noise and confounding components. In particular, the causal dominance condition holds:

$$\|\mathbf{c}_Z\| \gg \max(\|\mathbf{c}_E\|,\ \|\mathbf{c}_N\|)\,. \tag{37}$$

Consequently, since the causal component dominates the residuals in magnitude, the reconstructed representation is primarily governed by $\mathbf{c}_Z$, yielding:

$$\mathbf{Q} \;\approx\; \mathbf{c}_Z, \tag{38}$$

Stage II (Learn causal representations.) In the second attention layer, the original features $\mathbf{P}$ query the filtered bottleneck $\mathbf{Q}$ to reconstruct a causally grounded representation:

$$\mathbf{Z}_{\mathbf{P}} \;=\; \mathrm{LWA}(\mathbf{P}, \mathbf{M}, \mathbf{Q}) \tag{39}$$

i.e., the reconstruction is primarily guided by the causal semantics encoded in Q, so that $\mathbf{Z}_{\mathbf{P}}$ is dominated by the causal subspace and any residual leakage from confounding/noise is negligible.

Consequently, compared with the raw input $\mathbf{P} = \mathbf{C}+\mathbf{N}+\mathbf{E}$, the output $\mathbf{Z}_{\mathbf{P}}$ achieves enhanced causal fidelity by substantially reducing the relative contribution of non-causal components through the mediator-aligned dual-attention procedure. □

APPENDIX S3. EXTENDED THEORETICAL RESULTS

Assumption S1 (Sufficient Model Convergence)**.** We assume that the model optimization reaches a converged state where the minimal information loss ϵ incurred by the fusion module is smaller than the causal information gain δ. Specifically, we assume $\epsilon < \delta$.

Assumption S2 (Cross-Scale Complementarity and Information-Preserving Fusion)**.** Let Z_v denote the visual latent causal pathology state. We posit that the local view $\mathbf{f}_{loc}$ and global view $\mathbf{f}_{glb}$ are complementary: they individually retain non-negligible ambiguity ($H(Z_v \mid \mathbf{f}_{loc}) \geq \delta_{loc}$ and $H(Z_v \mid \mathbf{f}_{glb}) \geq \delta_{glb}$), whereas their joint observation significantly reduces uncertainty ($H(Z_v \mid \mathbf{f}_{loc}, \mathbf{f}_{glb}) \leq \delta_{joint}$), satisfying $\delta_{joint} \ll \min(\delta_{loc}, \delta_{glb})$.

Furthermore, we assume the LGCA fusion Φ is approximately information-preserving. Specifically, the mediator $M_v = \Phi(\mathbf{f}_{loc}, \mathbf{f}_{glb})$ captures the joint information within a margin $\epsilon_\Phi \geq 0$:

$$H(Z_v \mid M_v) \leq H(Z_v \mid \mathbf{f}_{loc}, \mathbf{f}_{glb}) + \epsilon_\Phi. \tag{40}$$

Theorem S3 (Dominance of the Fused Mediator)**.** *Under Assumption S2, the fused mediator M_v strictly dominates any single-scale view regarding the mutual information with the causal state Z_v:*

$$I(M_v; Z_v) \;\geq\; \max\big(I(\mathbf{f}_{loc}; Z_v),\, I(\mathbf{f}_{glb}; Z_v)\big) \;+\; \Delta I, \tag{41}$$

where the information gain ΔI is bounded by:

$$\Delta I \;= \min(\delta_{loc}, \delta_{glb}) - \delta_{joint} - \epsilon_\Phi. \tag{42}$$

Consequently, by Assumption S1, the fusion yields a strictly positive information gain: $\Delta I > 0$. A detailed proof is provided in Appendix S3.1.

Assumption S4 (Cross-Modal Posterior Contraction)**.** Let Z_g denote the causal genomic driver to be extracted. Let h_g be the raw genomic representation, and let the context priors be $A_v := \mathbf{f}_{loc}$ (local visual prior) and $A_t := h_t$ (textual prior). We assume the context priors provide *non-redundant* information about Z_g, i.e.,

$$I(Z_g; A_v \mid h_g) \geq \delta_v > 0, \tag{43}$$

$$I(Z_g; A_t \mid h_g, A_v) \geq \delta_t > 0. \tag{44}$$

Assumption S5 (Assumption of Causal Completeness in GCP)**.** Denote the two-stage GCP outputs as $g^{(0)} = \mathrm{CLA}_v(h_g, A_v)$, and $M_g = \mathrm{CLA}_t(g^{(0)}, A_t)$. We assume the learned cross-attention blocks produce *approximately sufficient, context-conditioned* summaries of the joint evidence:

$$H(Z_g \mid g^{(0)}) \leq H(Z_g \mid h_g, A_v) + \epsilon_v, \tag{45}$$

$$H(Z_g \mid M_g) \leq H(Z_g \mid h_g, A_v, A_t) + \epsilon_t, \tag{46}$$

where $\epsilon_v, \epsilon_t \geq 0$ capture approximation/optimization errors and decrease as the context-conditioning objectives are optimized.

Theorem S6 (Sequential Anchoring Improves the Genomic Mediator)**.** *Under Assumptions S4–S5, the GCP mediator M_g is strictly more informative about the causal driver Z_g than using genomics alone. Specifically,*

$$I(g^{(0)}; Z_g) \geq I(h_g; Z_g) + \delta_v - \epsilon_v, \tag{47}$$

$$I(M_g; Z_g) \geq I(h_g; Z_g) + \delta_v + \delta_t - (\epsilon_v + \epsilon_t). \tag{48}$$

Consequently, by Assumption S1, the fusion yields a strictly positive information gain: $I(M_g; Z_g) > I(h_g; Z_g)$.

S3.1. Proof of Theorem S3

Here we provide the detailed derivation showing that the Local–Global Cross-Attention (LGCA) module reduces uncertainty about the latent pathology state Z_v.

Proof. We proceed in two steps: first establishing the superiority of the joint view, and then bounding the performance of the learned mediator.

Step 1: Information Gain of the Joint View. We show that the joint pair $(\mathbf{f}_{loc}, \mathbf{f}_{glb})$ contains strictly more information about Z_v than either view alone. Using the identity $I(A; Z_v) = H(Z_v) - H(Z_v \mid A)$, the information gain of the joint view over the local view is:

$$\begin{aligned} I(\mathbf{f}_{loc}, \mathbf{f}_{glb}; Z_v) - I(\mathbf{f}_{loc}; Z_v) &= \big[H(Z_v) - H(Z_v \mid \mathbf{f}_{loc}, \mathbf{f}_{glb})\big] - \big[H(Z_v) - H(Z_v \mid \mathbf{f}_{loc})\big] \\ &= H(Z_v \mid \mathbf{f}_{loc}) - H(Z_v \mid \mathbf{f}_{loc}, \mathbf{f}_{glb}) \\ &\geq \delta_{loc} - \delta_{joint}. \end{aligned} \tag{49}$$

Similarly, for the global view:

$$I(\mathbf{f}_{loc}, \mathbf{f}_{glb}; Z_v) - I(\mathbf{f}_{glb}; Z_v) \geq \delta_{glb} - \delta_{joint}. \tag{50}$$

Since Assumption S2 states that $\delta_{joint} \ll \min(\delta_{loc}, \delta_{glb})$, the joint pair strictly reduces the uncertainty regarding Z_v.

Step 2: Analysis of the LGCA Mediator. Next, we relate the LGCA output M_v to this joint information. Based on the fusion accuracy condition (Eq. 8), we lower-bound the mutual information of M_v:

$$\begin{aligned} I(M_v; Z_v) &= H(Z_v) - H(Z_v \mid M_v) \\ &\geq H(Z_v) - \big(H(Z_v \mid \mathbf{f}_{loc}, \mathbf{f}_{glb}) + \epsilon_\Phi\big) \\ &= I(\mathbf{f}_{loc}, \mathbf{f}_{glb}; Z_v) - \epsilon_\Phi. \end{aligned} \tag{51}$$

Combining (51) with (49), we derive the gain over the local view:

$$\begin{aligned} I(M_v; Z_v) - I(\mathbf{f}_{loc}; Z_v) &\geq \big(I(\mathbf{f}_{loc}, \mathbf{f}_{glb}; Z_v) - \epsilon_\Phi\big) - I(\mathbf{f}_{loc}; Z_v) \\ &\geq (\delta_{loc} - \delta_{joint}) - \epsilon_\Phi. \end{aligned} \tag{52}$$

Analogously, the gain over the global view is:

$$I(M_v; Z_v) - I(\mathbf{f}_{glb}; Z_v) \;\geq\; (\delta_{glb} - \delta_{joint}) - \epsilon_\Phi. \tag{53}$$

Combining these results yields the theorem's main inequality:

$$I(M_v; Z_v) \;\geq\; \max\big(I(\mathbf{f}_{loc}; Z_v),\, I(\mathbf{f}_{glb}; Z_v)\big) + \min(\delta_{loc}, \delta_{glb}) - \delta_{joint} - \epsilon_\Phi.$$

where the information gain ΔI is bounded by:

$$\Delta I \;= \min(\delta_{loc}, \delta_{glb}) - \delta_{joint} - \epsilon_\Phi. \tag{54}$$

This proves that as long as the fusion error is sufficiently small, the gain ΔI is strictly positive.

□

S3.2. Proof of Theorem S6

Proof. According to Assumption S4, the following entropy reduction inequalities hold:

$$H(Z_g \mid h_g, A_v) \leq H(Z_g \mid h_g) - \delta_v, \tag{55}$$

$$H(Z_g \mid h_g, A_v, A_t) \leq H(Z_g \mid h_g, A_v) - \delta_t. \tag{56}$$

a) Stage 1: Anchoring to Visual Evidence.: By Assumption S5 (Eq. (45)), the entropy of the causal driver given the visual-anchored token satisfies:

$$I(g^{(0)}; Z_g) = H(Z_g) - H(Z_g \mid g^{(0)}) \geq H(Z_g) - [H(Z_g \mid h_g, A_v) + \epsilon_v] = I(h_g, A_v; Z_g) - \epsilon_v.$$

By the chain rule of mutual information, we expand the joint information term:

$$I(h_g, A_v; Z_g) = I(h_g; Z_g) + I(A_v; Z_g \mid h_g).$$

Using the non-redundancy assumption from Eq. (43), we obtain:

$$I(g^{(0)}; Z_g) \geq I(h_g; Z_g) + \delta_v - \epsilon_v,$$

which proves inequality (47).

b) Stage 2: Further Refinement with Textual Prior.: Similarly, by Eq. (46) from Assumption S5:

$$I(M_g; Z_g) = H(Z_g) - H(Z_g \mid M_g) \geq H(Z_g) - [H(Z_g \mid h_g, A_v, A_t) + \epsilon_t] = I(h_g, A_v, A_t; Z_g) - \epsilon_t.$$

Applying the chain rule again to the tripartite joint information:

$$I(h_g, A_v, A_t; Z_g) = I(h_g; Z_g) + I(A_v; Z_g \mid h_g) + I(A_t; Z_g \mid h_g, A_v).$$

Substituting the non-redundancy lower bounds from Eq. (43)and Eq. (44), we obtain:

$$\begin{aligned} I(M_g; Z_g) &\geq I(h_g; Z_g) + \delta_v + \delta_t - \epsilon_t \\ &\geq I(h_g; Z_g) + \delta_v + \delta_t - (\epsilon_v + \epsilon_t). \end{aligned} \tag{57}$$

□

APPENDIX S4. ALGORITHM

Algorithm 1 MulCauRL Training

Input: Multimodal data $\{H, G, T\}$ and target label (y for classification or (t, δ) for survival)
Output: predicted label $\hat{Y}$ or risk score r
Feature Encoding:
Patch features $\mathbf{H} \leftarrow \mathrm{Enc}_v(S)$
Text feature $h_t \leftarrow \mathrm{Enc}_t(T)$;
Genomic feature $h_g \leftarrow \mathrm{Enc}_g(G)$
Attention and slide feature $(\mathbf{A}, h_v) \leftarrow \mathrm{MIL}(\mathbf{H})$
Select instances $(h_{\text{top}}, h_{\text{bottom}}) \leftarrow \mathrm{TopK}(\mathbf{A}, \mathbf{H}, k)$
Multimodal Causal Representation Learning:
Visual Causal Representation:
$f_{\text{loc}} \leftarrow h_{\text{top}}$
$f_{\text{glb}} \leftarrow \mathrm{SegPool}_{N_{\text{glb}}}\big(\mathrm{Mamba1D}(\mathbf{H})\big)$ using Eq. (7)
$M_v \leftarrow \psi(f_{\text{loc}}, f_{\text{glb}}) = \mathrm{MGAM}$ using Eq. (8)
$Q_v \leftarrow \mathrm{LWA}(M_v, P_v, P_v)$ using Eq. (15)
$Z_v \leftarrow \mathrm{LWA}(P_v, M_v, Q_v)$ using Eq. (16)
Genomic Causal Representation:
$M_g \leftarrow \mathrm{CLA}(\mathrm{CLA}(h_g, f_{\text{loc}}), h_t)$ using Eq. (11)
$Q_g \leftarrow \mathrm{LWA}(M_g, P_g, P_g)$ using Eq. (15)
$Z_g \leftarrow \mathrm{LWA}(P_g, M_g, Q_g)$ using Eq. (16)
Multimodal Causal Representation:
$P_{\text{full}} \leftarrow \mathrm{Concat}(Z_v,\ h_t,\ Z_g)$ using Eq. (17)
Training:
if classification **then**
$\mathcal{L}_{\text{total}}^{\text{cls}} \leftarrow \alpha\mathcal{L}_{\text{bag}} + (1-\alpha)\mathcal{L}_{\text{inst}} + \mathcal{L}_{\text{c-reg}}$ using Eq. (23)
Update model parameters by minimizing $\mathcal{L}_{\text{total}}^{\text{cls}}$
else
$\mathcal{L}_{\text{total}}^{\text{surv}} \leftarrow \alpha\mathcal{L}_{\text{bag}} + (1-\alpha)\mathcal{L}_{\text{inst}} + \mathcal{L}_{\text{cox}}$ using Eq. (25)
Update model parameters by minimizing $\mathcal{L}_{\text{total}}^{\text{surv}}$
end if

APPENDIX S5. EXTENDED EXPERIMENTAL DETAILS

S5.1. Extended Details of Datasets

The data used in our experiment comes from six primary sites of TCGA (Kidney, Lung, Breast, Stomach, Brain, and Colon), covering multiple corresponding cancer cohorts to construct a cross-organ evaluation benchmark. The specific statistical information and number of slices for each cohort are summarized in Table S2. Each whole-slide image is first partitioned into non-overlapping patches. These patches are then encoded using a pre-trained encoder to obtain patch-level representations, which are subsequently aggregated into slide-level bags for downstream modeling. Representative patient-level clinical descriptions and the cancer-specific gene sets used for genomic modeling are provided in Table S3 and Table S4.

TABLE S2
SUMMARY OF TCGA CANCER COHORTS USED IN THIS STUDY.

TCGA Cohort	Total WSIs	Primary Site
TCGA-KICH	121	Kidney
TCGA-KIRC	518	Kidney
TCGA-KIRP	294	Kidney
TCGA-LUAD	499	Lung
TCGA-LUSC	512	Lung
TCGA-BRCA (IDC)	724	Breast
TCGA-BRCA (ILC)	151	Breast
TCGA-STAD	346	Stomach
TCGA-GBM	257	Brain
TCGA-LGG	358	Brain
TCGA-COAD	315	Colon

TABLE S3
REPRESENTATIVE CLINICAL DISEASE DESCRIPTIONS OF DIFFERENT CANCER TYPES.

COHORT	CLINICAL DESCRIPTION
KIDNEY	HE IS A 38-YEAR-OLD MAN WITH A TUMOR IN THE RIGHT KIDNEY. PATHOLOGIC STAGING REVEALED STAGE II (T2 NX MX). LABORATORY TESTS SHOWED NORMAL SERUM CALCIUM, NORMAL HEMOGLOBIN, AND NORMAL WHITE BLOOD CELL COUNT.
BREAST	SHE IS A 50-YEAR-OLD ASIAN, NOT HISPANIC OR LATINO PATIENT. MENOPAUSE STATUS IS PREMENOPAUSAL (LESS THAN 6 MONTHS SINCE LAST MENSTRUAL PERIOD, NO PRIOR BILATERAL OVARIECTOMY, AND NOT ON ESTROGEN REPLACEMENT THERAPY). THE TUMOR IS LOCATED IN THE RIGHT BREAST. THE INITIAL PATHOLOGIC DIAGNOSIS WAS MADE IN 2010. PATHOLOGIC STAGE IS STAGE IIA WITH TNM CLASSIFICATION T2 N0 M0. BIOMARKER ASSESSMENT INDICATES ER POSITIVITY AND HER2 NEGATIVITY WITH AN IHC INTENSITY SCORE OF 1+. NO NEW TUMOR EVENT WAS OBSERVED AFTER INITIAL TREATMENT. THE PATIENT IS ALIVE AND TUMOR FREE.
LUNG	SHE IS A 75-YEAR-OLD WHITE, NOT HISPANIC OR LATINO PATIENT WITH A TUMOR LOCATED IN THE RIGHT LOWER LOBE OF THE LUNG. THE INITIAL PATHOLOGIC DIAGNOSIS WAS MADE IN 2012. PATHOLOGIC STAGE IS STAGE IA WITH TNM CLASSIFICATION T1A N0 M0, AND RESIDUAL TUMOR STATUS R0. THE PATIENT IS A FORMER SMOKER WHO QUIT WITHIN THE PAST 15 YEARS, WITH A SMOKING HISTORY OF 100 PACK-YEARS AND CESSATION IN 2002. PULMONARY FUNCTION TESTING WAS PERFORMED, WITH PRE- AND POST-BRONCHODILATOR FEV1 VALUES OF 115% AND 118%, FEV1/FVC RATIOS OF 77% AND 75%, AND A DLCO OF 48%. THE PATIENT IS ALIVE, TUMOR FREE, WITH 640 DAYS TO LAST FOLLOW-UP.

TABLE S4
CANCER-SPECIFIC GENE LISTS USED FOR GENOMIC MODELING ACROSS DIFFERENT PRIMARY SITES.

CANCER TYPE	SELECTED GENES
KIDNEY	VHL, TP53, PTEN, MET, CDKN2A, SETD2, TFE3, FH, PBRM1, BAP1, KDM5C, MTOR
BREAST	TP53, PIK3CA, GATA3, MAP3K1, CDH1, PTEN, ERBB2, BRCA1, BRCA2, BAP1, PBRM1, KDM5C, MTOR, TBX3, FOXA1, ESR1
LUNG	AKT1, ALK, ARID1A, BRAF, CD274, CDKN2A, CREBBP, CXCL13, EGFR, EP300, ERBB2, FGFR1, HRAS, IFNG, IRF1, JAK2, KEAP1, KMT2D, KRAS, MET, NF1, NFE2L2, NLRP3, NRAS, NTRK1, PIK3CA, PTEN, RB1, RBM10, RET, ROS1, SETD2, SMARCA4, SMARCB1, SOX2, STAT3, STK11, TP53
STOMACH	TP53, CDH1, ARID1A, MLH1, MSH2, CTNNA1, KRAS, BRAF, EGFR, PIK3CA, MET, RHOA, APC, SMAD4, CDKN2A, CLDN18, GNAS, ERBB2, FGFR2, AKT1
COLON	APC, CTNNB1, AXIN2, KRAS, NRAS, BRAF, EGFR, ERBB2, PIK3CA, PTEN, SMAD4, TGFBR2, MLH1, MSH2, MSH6, PMS2, TP53, FBXW7, SOX9, MYC
BRAIN	TP53, IDH1, EGFR, PTEN, MGMT, ATRX, TERT, NF1, RB1, PIK3CA, PDGFRA, TPR, TPX2, HIF1A, ALDH1L1