PERRIN CONFERENCES

TALC LITIGATION CONFERENCE

The Midland Hotel, Chicago | June 4, 2026

Science and Genetics: Where Are We Today?

Peter Andersen Moir, Esq.
Morgan Lewis
Dallas, TX

Michael C. Cooney, Esq.
Cooney & Conway
Chicago, IL

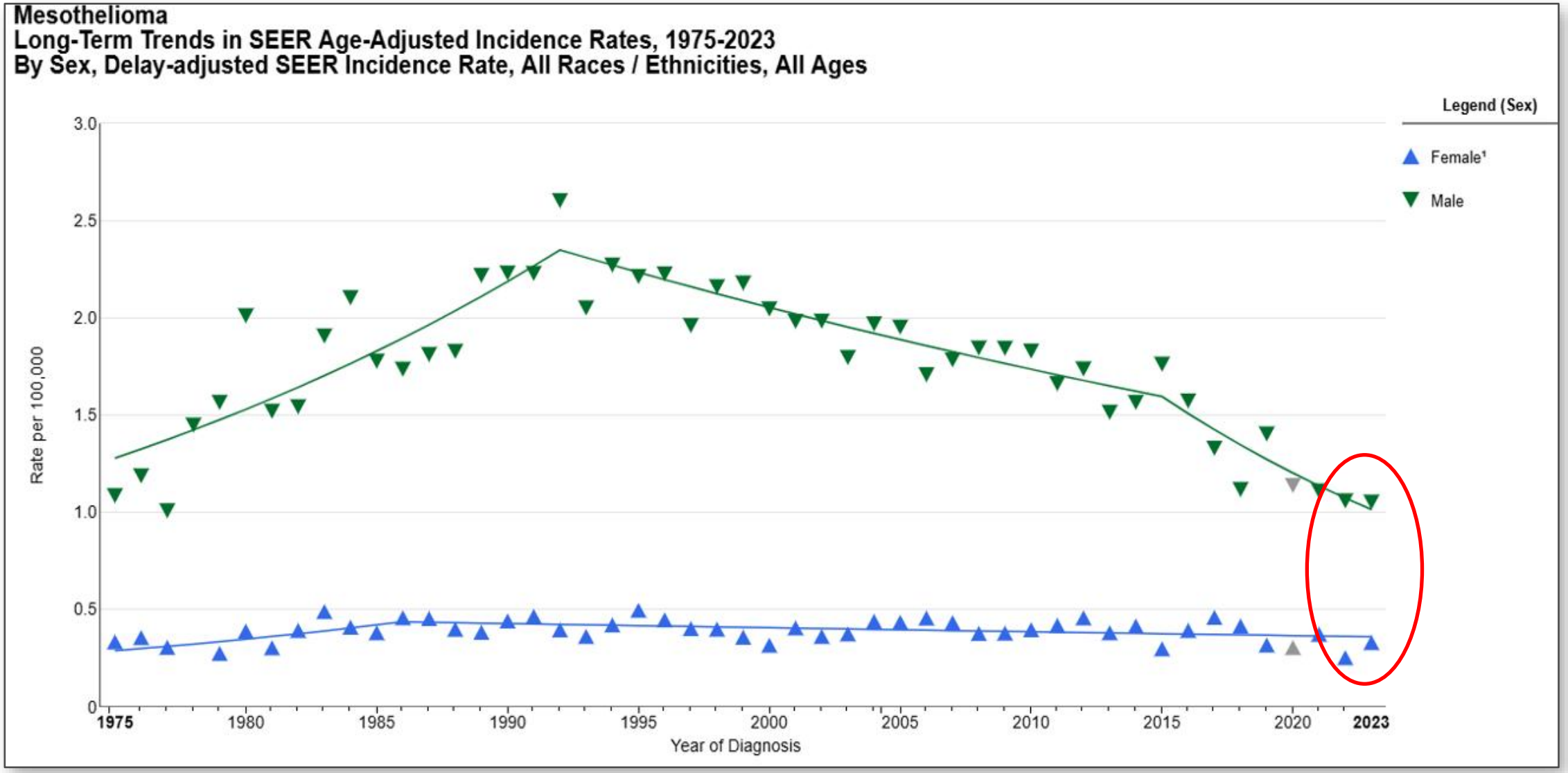
John D. Cosmich, Esq.
Cosmich
Jackson, MS

Emily Goswami, MS, CIH
Principal Scientist
Roux
Oakland, CA

Ellis et al., 2026: Pressed Powder Exposures

- Average respirable dust level: 0.002 mg/m^3
- Average duration of application: 6.35 min
- Average mass of product used: 0.01-0.08 g
- No asbestos fibers were detected by NIOSH 7402 (TEM)

National Cancer Institute, 2026: Mesothelioma Incidence Data



IARC 2025: Revised Talc Monograph

	IARC 2010	IARC 2025
Overall	Group 2B – Possible	Group 2A – Probable
Cancer in humans	Limited (Perineal) Inadequate (Inhalation)	Limited
Cancer in animals	Limited	Sufficient
Mechanistic data	NA	Strong

IARC 2025: Revised Talc Monograph

IARC 2010: Group 2B – Possibly Carcinogenic

- Perineal use of talc-based body powder = Group 2B
- Inhaled talc not containing asbestos or asbestiform fibers is not classifiable in regard to human carcinogenicity (Group 3)

IARC 2025: Group 2A – Probably Carcinogenic

- Positive association between perineal talc use and ovarian cancer
  - Bias from exposure misclassification and/or asbestos in talc
- No conclusions on causal relationship for uterine cancer
- No convincing evidence for causal relationship:
  - Stomach cancer
  - Lung cancer
  - Mesothelioma and other cancers

Why the Changes?

- No major new studies published
- Interpretation of existing animal data
  - Adrenal pheochromocytomas (tumors of the adrenal gland, usually benign)
- IARC methodology incorporating mechanistic data

Korchevskiy & Wylie, 2025: IARC Critique

CRITICAL REVIEWS IN TOXICOLOGY
https://doi.org/10.1080/10408444.2025.2585870

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REVIEW ARTICLE

OPEN ACCESS Check for updates

The IARC re-classification of talc carcinogenicity: a move in the wrong direction?

Andrey A. Korchevskiy[a] and Ann G. Wylie[b]

[a]Chemistry & Industrial Hygiene, Inc, Lakewood, CO, USA; [b]University of Maryland, College Park, MD, USA

ABSTRACT

The paper explores a content of the recent International Agency for Research on Cancer (IARC) Monograph (Volume 136) where pure talc was reclassified from the Group 2B ("Possibly carcinogenic to humans") to the Group 2A ("Probably carcinogenic to humans"). The Monograph is considered in the context of the history of the IARC program for classification of carcinogens as well as in the framework of basic principles of toxicological science. It is demonstrated that reclassification was made not based on any new scientific information available, but rather because of a change in some of the methodological approaches or preferences employed by IARC. In particular, it is demonstrated that there are significant mineralogical issues in characterization of talc by the recent IARC Monograph. It is shown why weight-of-evidence for carcinogenicity of pure talc in experimental animals cannot be estimated higher than "limited", and in human study higher than "inadequate". It will also be argued that utilization of separated mechanistic criteria (key characteristics of carcinogens) without contextual analysis and proven mode-of-action (MoA) can cause significant uncertainties in the determination of carcinogenicity in humans. There is a need for comprehensive risk assessment for various agents and processes, rather than just hazard identification that the IARC continues to exercise with questionable relevance for global cancer prevention.

Abbreviation: AOP: adverse outcome pathways; IARC: International Agency for Research on Cancer; IRIS: Integrated Risk Information System; KC: key characteristic; MoA: mode-of-action; MTD: maximum tolerated dose; NAM: new approach method; NF-κB: nuclear factor kappa-light-chain-enhancer of activated B cells; NTP: National Toxicology Program; PCA: principal component analysis; SVF: synthetic vitreous fibers; US EPA: United States Environmental Protection Agency; CART: Classification and Regression Trees methodology

ARTICLE HISTORY
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KEYWORDS
talc; IARC; carcinogenicity; classification; mechanistic criteria; mode-of-action (MoA)

Seyyedsalehi et al., 2026: Meta-analysis

Cancer Type	No. of Studies	Pooled Relative Risk (RR)	Notes
Mesothelioma	8	NA	No mesothelioma cases were reported among talc miners and millers
Lung Cancer	13	1.13 (95% CI: 0.97-1.33) for miners and millers 1.12 (95% CI: 0.79-1.57) for other workers	No statistically significant increased risk
Laryngeal Cancer	7	0.98 (95% CI: 0.58-1.57)	No association with talc exposure

Conclusions: Current evidence does not support increased risks of lung, mesothelioma, or laryngeal cancers among workers exposed to asbestos-free talc, future studies should better control for confounders, especially tobacco smoking.

Roggli et al., 2025: Lung Fiber Burden in Peritoneal Mesotheliomas

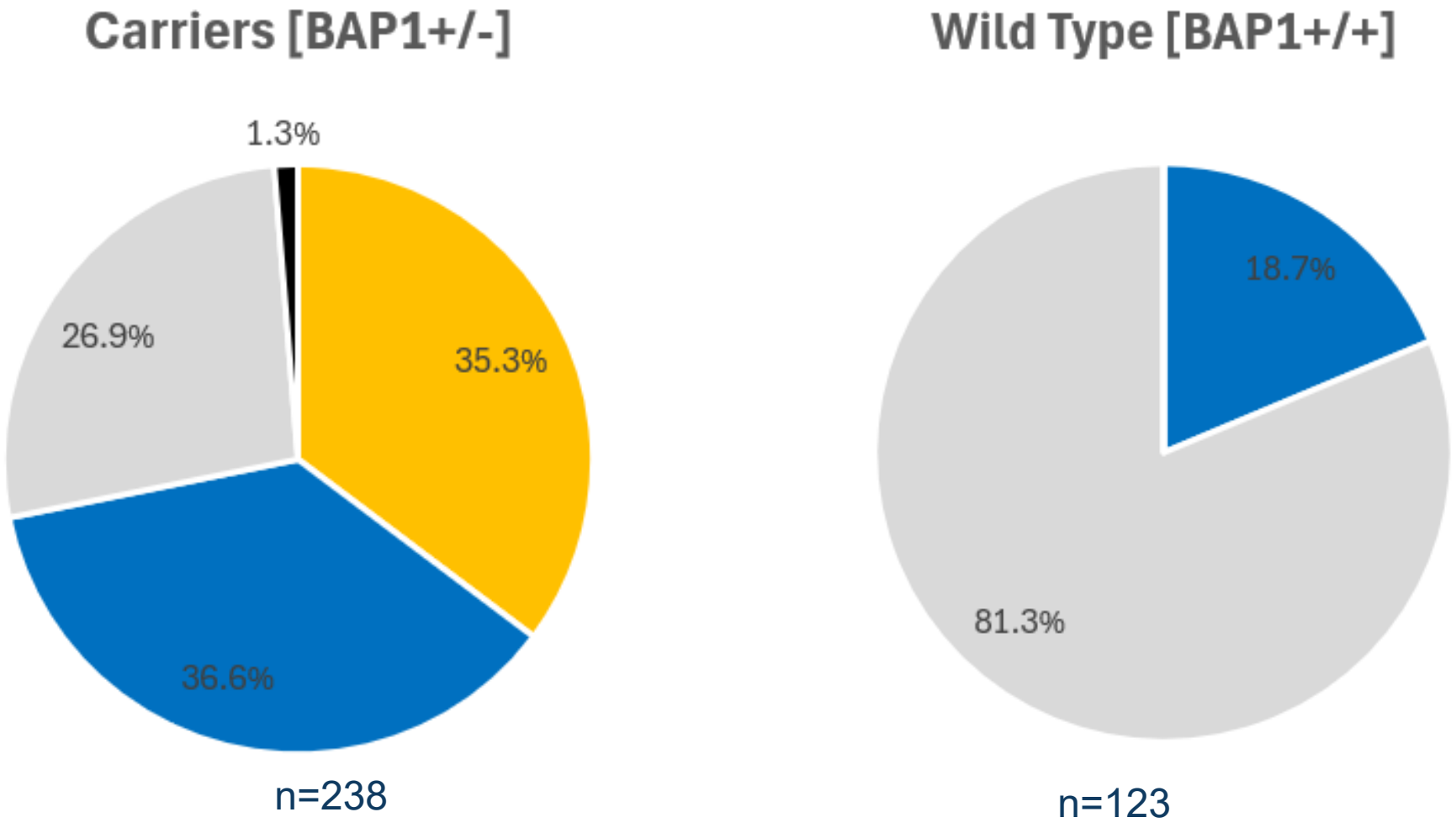
Table 1. Demographic information on 10 patients with peritoneal mesothelioma and a lung fiber burden analysis since 1/1/2010.

	Age/gender	Histologic type	PPP	Exposure information
Case 1	75/M	Epithelial	Y	Micronite filter cigarette mfg. plant
Case 2	75/M	Epithelial	Y	Insulator
Case 3	62/M	Biphasic	N	Electrician
Case 4	63/M	Epithelial	ND	Carpenter/power plant architect
Case 5	53/M	Biphasic	N	Auto mechanic
Case 6	61/M	Biphasic	N	HHC (father – vehicle mechanic)
Case 7*	63/F	Epithelial		
Case 8	62/F	Biphasic		
Case 9	39/F	Epithelial		
Case 10#	48/F	Biphasic‡		

*Patient also had adenocarcinoma of right lung, angiomyolip
#Patient with endometriosis.
‡HHC=household contact; ND=no data; PPP=parietal pleural

In conclusion, our findings indicate that most peritoneal mesothelioma cases since 2010 are not asbestos related based on fiber analysis of lung tissue samples. Determination of causation in present day peritoneal mesothelioma cases requires careful consideration of the patient's potential asbestos exposure history, prior radiation therapy, prior chronic peritoneal inflammatory conditions, and possible germline mutations that may predispose the individual to the development of mesothelioma.

Carbone et al., 2025: BAP1 Mutations



Carbone et al., 2025: BAP1 Mutations

Key Characteristics among MM:

- **1 of 84** had evidence of asbestos exposure
- Younger in age (median age = **54**)
- **45.2%** developed multiple cancers
- Distinct appearance and histologic features
- Remain slow growing for years and do not require as aggressive therapy
- Median survival of **7 years**
- “Low-grade-germline-mutant-BAP1-associated-mesotheliomas, L-BAM”

Genetics and Mesothelioma: Science Comes to the Litigation, not the Litigation Goes to Science

- The link between genetic mutations and mesothelioma developed independently from the litigation
  - Link was developed entirely with funding from NCI
- It is not science that developed in response to the litigation, such as:
  - Studies of litigation cases
  - Studies of products/exposures at issue in asbestos/talc litigation
  - Epidemiology studies of exposures to talc
  - Fiber digestion studies

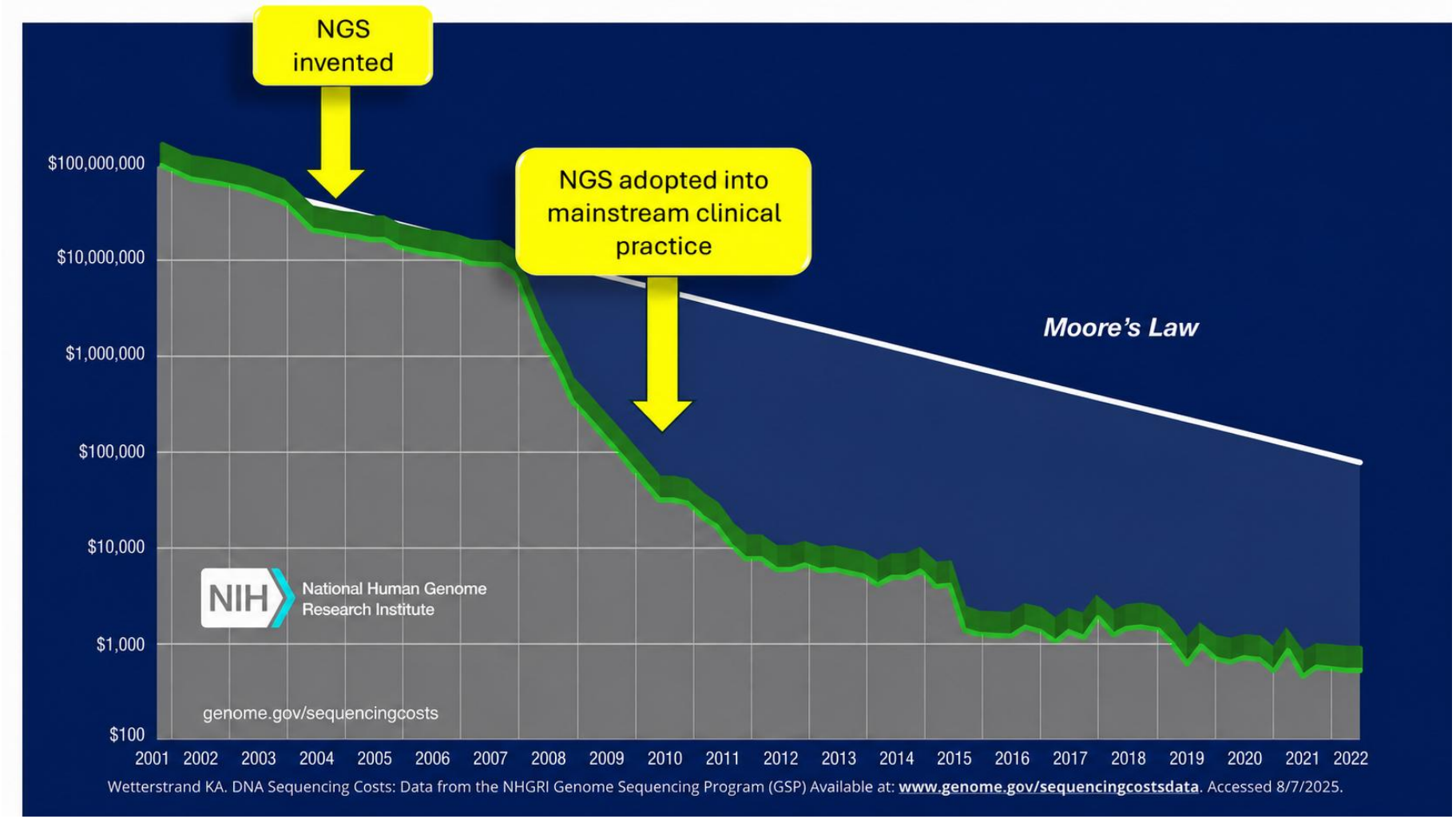
Inherited Genetic Mutations are at Issue Only in a Minority of Mesotheliomas

- 10-15% or more of all mesothelioma cases diagnosed today
- 50% or more of mesotheliomas diagnosed under age 55 or with strong family history of cancer
- As the number of mesotheliomas continues to decrease over time because of workplace control measures, the percentage of mesotheliomas with inherited pathogenic mutations likely will increase

Why Genetics is an Issue in Mesothelioma Causation Today but was Unheard of 15 Years Ago

- First mapping of human genome:
  - Finally Completed in 2001
  - Total time to map 1 human genome: 13 years
  - Cost: $1 billion
- To sequence 1 person's genome today:
  - Cost: $1,000
  - Time: A few hours

Cost of Sequencing per Human Genome



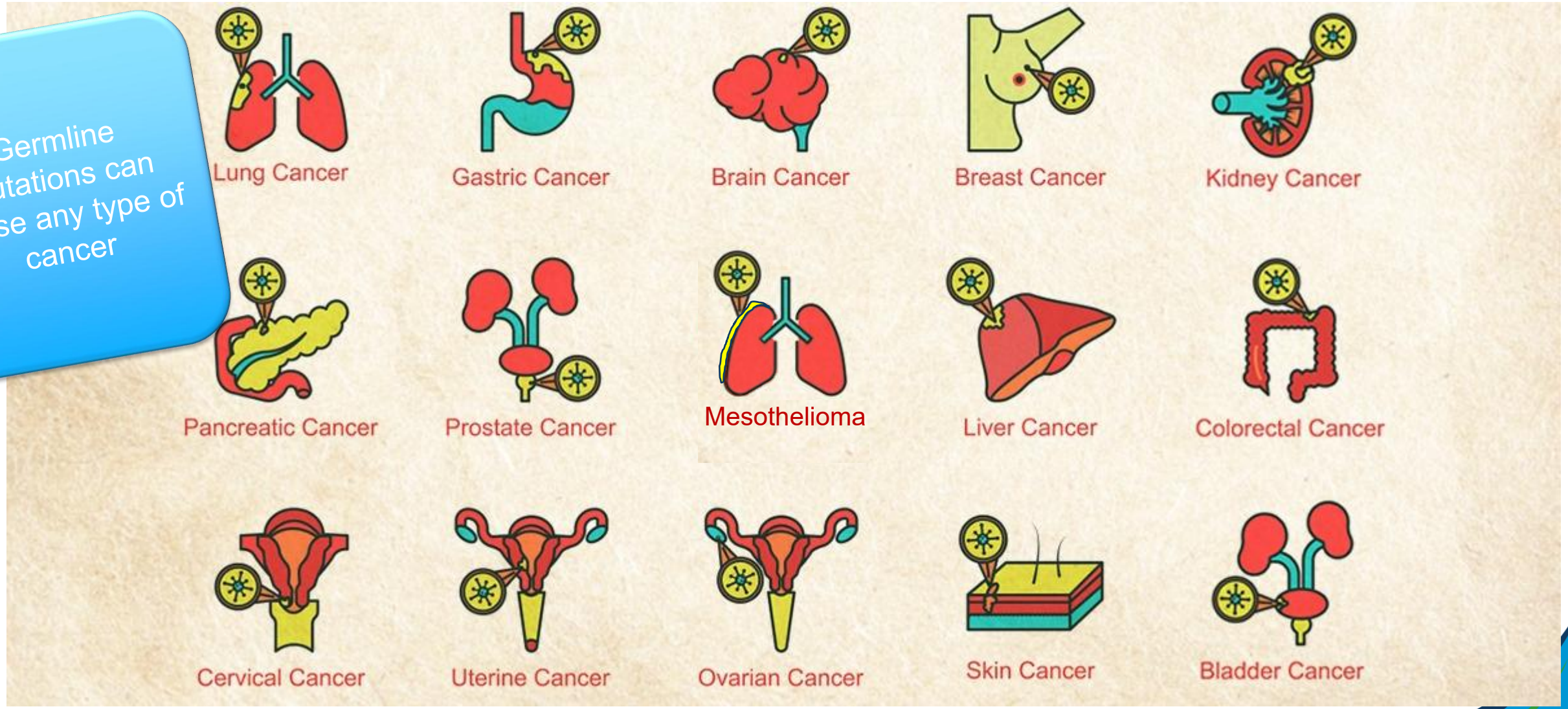
Why Is Sequencing Important in Determining Mesothelioma Causation?

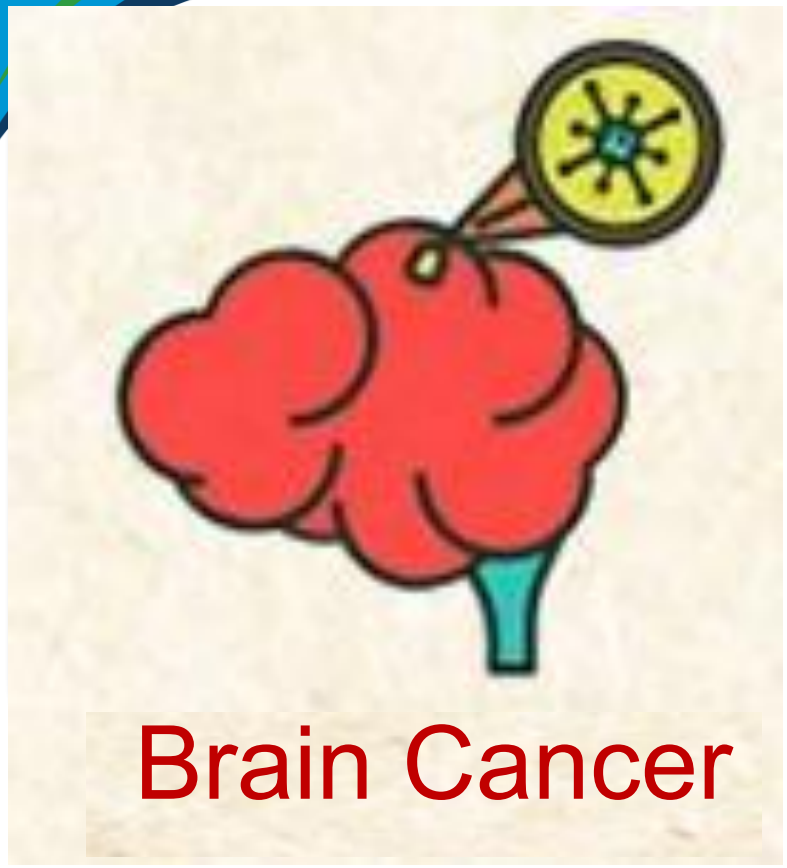
- Sequencing can tell us:
  - What pathogenic (i.e., disease-causing) mutations are present in the person's mesothelioma cells
  - What pathogenic mutations are inherited (when sequencing non-cancer cells)
  - The pattern of genetic damage present in cancer cells

- Identification of pathogenic mutations is critically important to:
  - Patient (potential therapy)
  - Family members (monitoring/early detection)

Cancer type tells you what cell it starts in - Not what caused it

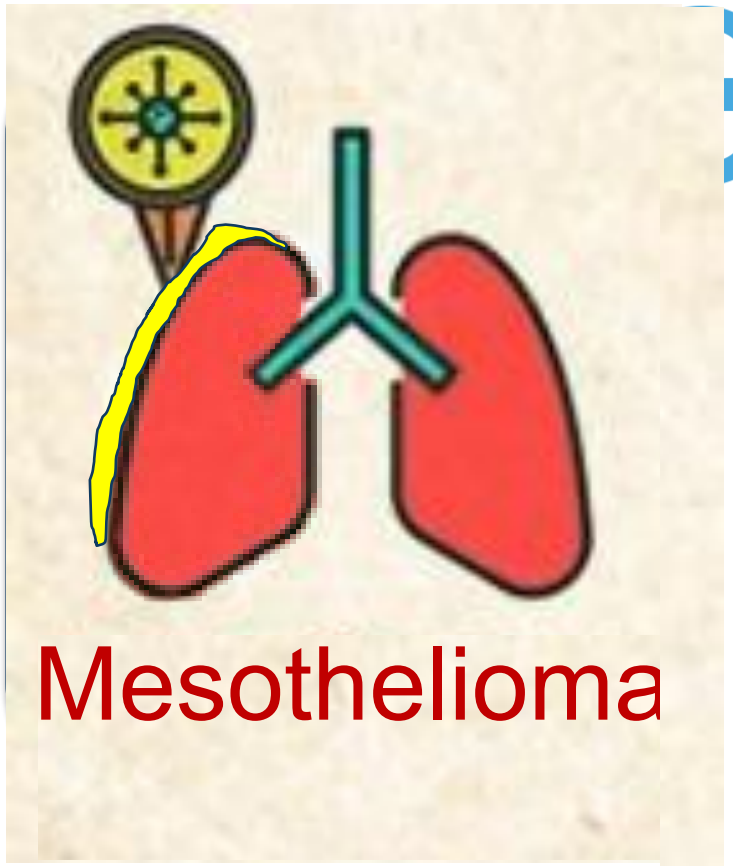
Germline mutations can cause any type of cancer





Brain Cancer

Lung Cancer



Mesothelioma

Same type of cancer but different causes

Mutations matter!

A Check List To Distinguish Mesotheliomas Caused In Whole Or In Part By Asbestos From Mesotheliomas Caused Only By An Inherited Pathogenic Mutation

Typical Characteristics of Two Different Diseases

	Mesothelioma caused by asbestos	*Mesothelioma caused by inherited mutation*
Family History of Cancer	**NO**	**YES**
Younger Patients *(under 55)*	**NO**	**YES**
Very Invasive	**YES**	**NO**
Lots of Genetic Damage	**YES**	**NO**
Medical Evidence of Asbestos Exposure	**YES**	**NO**
Survival Timeframe	**SHORT**	**LONG**
Resistant to Treatment	**YES**	**NO**

Does an Inherited Mutation Make Us More Susceptible to Getting Mesothelioma from Asbestos?

- Of course it does, provided:
  - Sufficient exposure to asbestos to cause chronic inflammation at cancer site
  - There is objective medical evidence of exposure

- Susceptibility does not mean asbestos played any part in causing the mesothelioma
  - Walk through the check list:
    - If asbestos played any role, it will check boxes of asbestos-caused mesothelioma

Molecular Pathology Can Distinguish Asbestos Mesotheliomas from Non-Asbestos Mesotheliomas

- Old science: Examining mesothelioma cells cannot tell us what caused them to turn into cancer cells

- New science: Molecular sequencing tells us what mutations and genetic damage are present in cancer cells
  - Molecular studies describe the pattern of mutations and genetic changes present in asbestos-caused mesotheliomas
  - If those mutations/changes are absent, molecular pathology can rule out asbestos as a cause of the mesothelioma

Molecular Pathology Check List: Cancer Cells In Asbestos-Caused Mesotheliomas Have A Lot Of Certain Types of Genetic Damage

Typical Genetic Damage in Mesothelioma Cells Caused by Asbestos

	Asbestos Tumors	Non-Asbestos Tumor
More than 10 mutations	✓	✗
Chromothripsis	✓	✗
Large deletions	✓	✗
HRD-positive signature	✓	✗
Aneuploidy	✓	✗
BAP1, NF2, SETD2, and other somatic mutations	✓	✗
Pathogenic Germline mutation in tumor suppressor gene	✗	✓

The Method For Determining Cancer Causation Is Evolving

- For many years, cancer causation was determined using the 1965 Bradford Hill Criteria
  - Relied heavily on epidemiology
- As a result of scientific advancements, 2004 NCI Panel revised cancer causation criteria to rely on biological evidence from the patient, not just epidemiology
- Today, modern molecular sequencing is rendering all these criteria obsolete
- Applies to all cancers
  - Mesothelioma is a cancer like all other cancers

Molecular Pathology and Genetic Sequencing Can And Will Determine Causation, Including For Mesothelioma

- Molecular pathology and genetic sequencing can and will tell us if asbestos played any part in causing a patient's mesothelioma
  - They already do in some cases
  - They provide objective evidence of causation
  - Rapidly expanding use:
    - Molecular pathology/genetic sequencing are becoming the standard of care

New science? Or same science applied to different genes?

- Which genes are we talking about?
- Carbone's research dating back to 2010 and before talks about BAP-1.
  - Cappadocia – BAP-1 plus erionite = very high rate of MM
  - Body of research relied upon shows that gene times environment = disease

References:

1. Lee M, Alexander HR, Burke A. Pathology 2013
2. Liu S, Staats P, Lee M, Alexander HR, Burke AP Pathology 2014
3. Pastorino S., et al., JCO 2018
4. Carbone M et al., JTO 2022
5. Betti et al., Cancer Letters 2017
6. Panou et al JCO 2018
7. Malpica A et al., Am J Surgical Pathol 2021

- None of reliance materials say genetic mutation alone causes MM

2021

Mesothelioma in immigrants from Turkey: Genes have a minor role

Selma Metintas [a,b], Muzaffer Metintas [b,c,*], Guntulu Ak [b,c], Gunnar Hillerdal [d,e], Hirsh Koyi [d,e,f]

Results: The cohort consisted of 337 people, 203 of whom were born and/or lived in Karain before immigrating to Sweden (erionite-exposed), and 134 who were born in Stockholm (erionite-unexposed). There were 69 deaths, 42 (61%) due to mesothelioma, and two patients with the disease who were still alive. Of these 44 patients, 22 were men. All mesothelioma patients were in the erionite-exposed group. In the age group 30–49 years, mesothelioma developed in 11 of 38 (29%) with erionite exposure, while there were no cases among 86 persons in the non-exposed group. For men, the AAMIR was 253.9 per 100,000 persons in the whole cohort, and for women, it was 350.9. The mSIR was 71.9 for men and 393.1 for women. Exposure to erionite exceeding 20 years and age over 40 years were associated with increased mesothelioma risk.

Conclusion: Exposure to erionite is the leading cause of mesothelioma in Karain villagers, and genetic factors are probably of minor importance.

Carbone 2025 – New Disease?

- Carbone 2025 – L-BAM “Low grade germline-mutant *BAP-1*-associated Mesothelioma.”

CONCLUSION: Compared to sporadic MM, MM developing in *BAP1*$^{+/-}$ carriers are a different disease, biologically, histologically and clinically: these patients require a tailored clinical approach. Because these patients are at high risk of developing multiple cancers, they benefit from annual screening for early cancer detection that can be life-saving.

Carbone 2025 – Apply findings of BAP-1 to other genes

- Experts have relied on these conclusions to claim that other germline genetic mutations can cause MM by themselves. (BRCA1, BRCA2, MUTYH, etc.)
- Currently no real epidemiology to support this:
  - 3 total BRCA1 MM in the reliance materials, all with asbestos exposure.

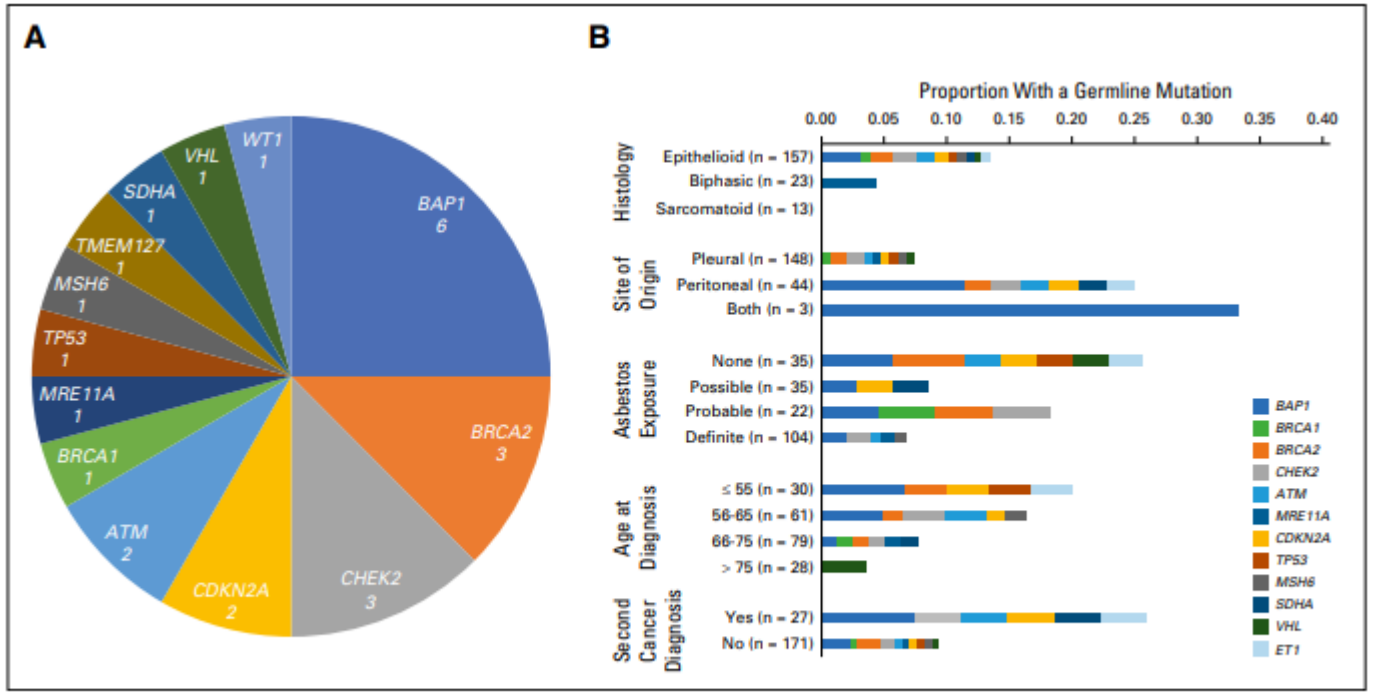


Fig 1. Germline cancer susceptibility gene mutations identified in patients with malignant mesothelioma. (A) Distribution of the 24 mutations identified in 23 patients among 13 genes. (B) Proportions of patients with a germline mutation by specific clinical characteristics.

Results from Panou 2018 study of patients at the University of Chicago Hospital

Carbone 2025 – No Asbestos Exposure?

Results: We identified 34 different germline inactivating mutations. Among 238 *BAP1*$^{+/-}$ carriers aged 27-81, 84 were diagnosed with mesothelioma (35%), 1/84 had evidence of asbestos exposure. No mesothelioma was recorded among 123 siblings/relatives who did not inherit *BAP1*$^{+/-}$

- Does not use questionnaires for self-reported exposures to asbestos in his studies, does not investigate whether someone was exposed via IH, and does not ask about talc exposures.
- Only examines the radiology and medical records for objective markers in his study, a significant departure from past practices.

Genetics as sole cause of MM – New science or hypothesis?

STEPHEN ANGELLOZ

VERSUS

TAYLOR-SEIDENBACH, INC., ET AL

* *

COURT'S RULING ON PLAINTIFF'S MOTIONS IN LIMINE

THURSDAY, APRIL 9, 2026

THE HONORABLE D. NICOLE SHEPPARD

JUDGE PRESIDING

Genetics as sole cause of MM – New science or hypothesis?

-Dr. Mutti, relying on Carbone
2025, excluded under *Daubert*

The defendants have failed to point to studies that were specifically designed to examine the general causation theory that a genetic mutation is independently capable of causing mesothelioma.

This Court finds that there are -- there were sufficient -- or insufficient evidence provided that would support the theory that Dr. Mutti promotes, and therefor finds that the plaintiff's *Daubert/Foret* motion in limine to exclude and/or limit the testimony of Dr. Luciana Mutti is hereby granted.

Spontaneous Mesotheliomas in Germline *Bap1* Heterozygous Mice from Different Genetic Backgrounds

Yuwaraj Kadariya [1,†], Li Zhang [2,†], Eleonora Sementino [1], Eric Ross [2] and Joseph R. Testa [1,*]

- Mice followed for up to 31 months- follow up to 2016 kadariya paper
- Only 2/329 bap1 mutant developed meso in absence of asbestos exposure
- 0/227 wild-type mice developed meso in absence of asbestos exposure
- No statistically significant difference in meso rates between the two using bayesian analysis

2025

Spontaneous Mesotheliomas in Germline *Bap1* Heterozygous Mice from Different Genetic Backgrounds

Yuwaraj Kadariya [1,†], Li Zhang [2,†], Eleonora Sementino [1], Eric Ross [2] and Joseph R. Testa [1,*]

5. Conclusions

Using multiple statistical approaches, our results did not detect a significant difference between the probabilities of mesothelioma occurrence in *Bap1*-mutant and WT mice. Thus, we cannot conclude that germline *Bap1* heterozygous mice have an increased risk of spontaneous mesothelioma compared to WT mice. However, given that even trace amounts of asbestos induce a high incidence of mesothelioma in *Bap1*-mutant mice compared to WT mice [4,6], this suggests that germline *Bap1* mutations create a highly susceptible setting for a gene-environment interaction with deadly consequences. This aligns with the interplay between mutant cancer predisposition genes and asbestos, particularly low exposures, which have been documented in mesothelioma patients [27,28].

2025

Molecular Pathology

- “Mutational landscape” of the tumor can tell us whether it is being driven by tumor suppressor gene or asbestos.
- Dr. Neff – relying on findings of previous studies (Bueno 2016, Hmeljak 2018, Mangiante 2023 for pleural Mesos; Joseph 2017, Hung 2020, and Offin 2022 for peritoneal Meso) for support.
- Examines mutational landscape for asbestos v. non-asbestos mesos based on these studies alone. Only works if these authors are correct in their analysis of asbestos v. non-asbestos.
- No mutational signature for asbestos-caused mesothelioma
  - Most common somatic mutation is BAP1, only present in 26.66% of asbestos caused mesos.
- Dr. Tomlins – Also admits no mutational signature for mesothelioma.
- Not written about in peer reviewed literature
- Alternative theories – younger clients respond better to treatment, bodies natural defenses prevent invasion into tissue, modern medicine (HIPEC, chemo, immune, etc.) provide for considerably better treatment outlook.

References

1. Carbone, M., Minaai, M., Kittaneh, M., Krausz, T., Miettinen, M. M., Hammarström, Q. P., ... & Yang, H. (2025). Clinical and pathologic phenotyping of mesotheliomas developing in carriers of germline BAP1 mutations. Journal of Thoracic Oncology, 20(11), 1683-1698. https://doi.org/10.1016/j.jtho.2025.06.020

2. Ellis, J., Spaeth, C., Gallagher, A., Ellis, B., Rosen, E., & Holton, M. (2026). Airborne dust exposure during the application of talc-based pressed powder makeups. Journal of Occupational and Environmental Hygiene, 1-14. https://www.tandfonline.com/doi/full/10.1080/15459624.2025.2609708

3. IARC (2025). Talc and acrylonitrile. IARC Monogr Identif Carcinog Hazards Hum. 136:1–805. Available from: https://publications.iarc.who.int/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Talc-And-Acrylonitrile-2025

4. Korchevskiy, A. A., & Wylie, A. G. (2025). The IARC re-classification of talc carcinogenicity: a move in the wrong direction?. Critical Reviews in Toxicology, 55(9), 867-889. https://www.tandfonline.com/doi/pdf/10.1080/10408444.2025.2585870

5. Roggli, V. L., Novakovic, S., Ghio, A. J., Li, H., Pina-Oviedo, S., Carney, J. M., ... & Pavlisko, E. N. (2025). Recent trends in the causation of peritoneal mesothelioma: fiber burden analysis of ten cases. Ultrastructural Pathology, 49(3), 288-295. https://www.tandfonline.com/doi/full/10.1080/01913123.2025.2483226

6. SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute; 2026 Apr 22. [cited 2026 May 8]. Available from: https://seer.cancer.gov/statistics-network/explorer/ . Data source(s): SEER Incidence Data, November 2025 Submission (1975-2023), SEER 8 registries.

7. Seyyedsalehi, M. S., Powley, W. A., & Boffetta, P. (2026). Occupational exposure to asbestos-free talc and risk of respiratory cancers, including larynx, lung and mesothelioma: a systematic review and meta-analysis. Journal of Thoracic Oncology, 103710. https://linkinghub.elsevier.com/retrieve/pii/S1556086426001632

Thank You!

Emily Goswami, CIH
Principal Scientist
Oakland, CA
egoswami@rouxinc.com