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SCUOLA DERMATOLOGICA
S E R G I O C H I M E N T I



Evento accreditato ECM

ROMA, 6 DICEMBRE 2019

TECNOLOGIA e INNOVAZIONE TERAPEUTICA in DERMATOLOGIA

NH Collection Roma Centro Via dei Gracchi 324, Roma

Responsabili scientifici

Ketty Peris, Luca Bianchi, Maria Concetta Fargnoli

Segreteria Organizzativa



Università di Roma



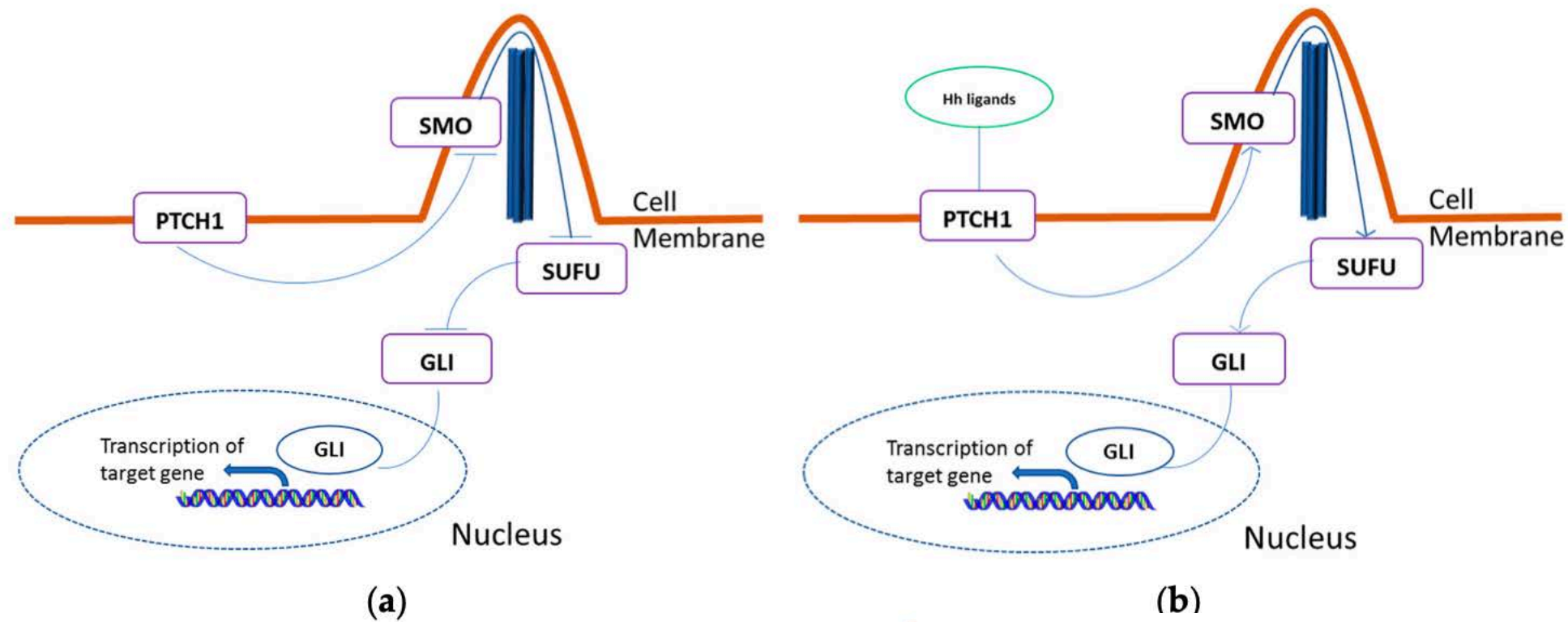
TERAPIA DEL CARCINOMA BASOCELLULARE AVANZATO: CASISTICA CLINICA

Mauro Mazzeo
Dipartimento di Dermatologia e Venereologia
Policlinico Tor Vergata

Review

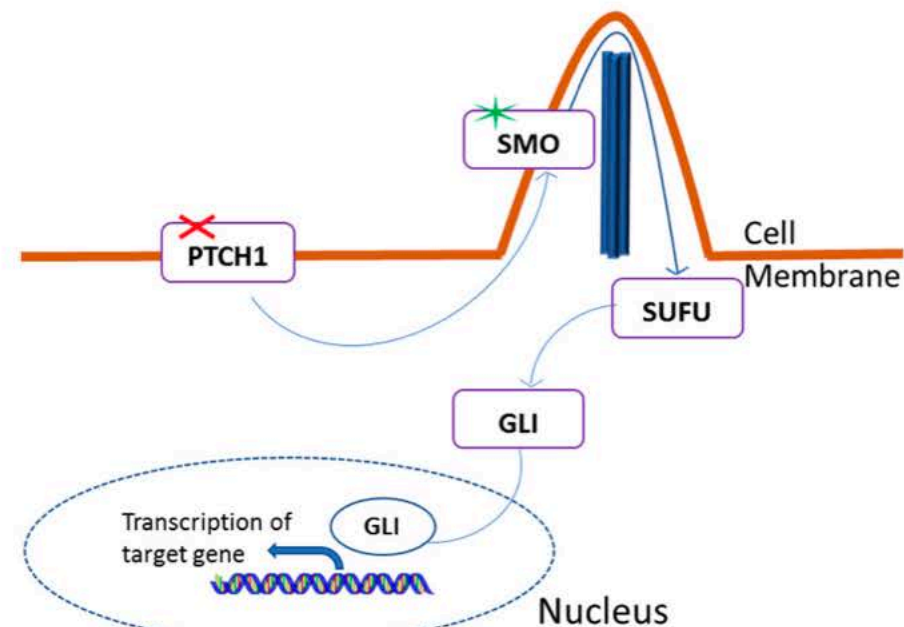
Understanding the Molecular Genetics of Basal Cell Carcinoma

Cristina Pellegrini [†] , Maria Giovanna Maturo [†], Lucia Di Nardo , Valeria Ciciarelli, Carlota Gutiérrez García-Rodrigo and Maria Concetta Fagnoli ^{*}



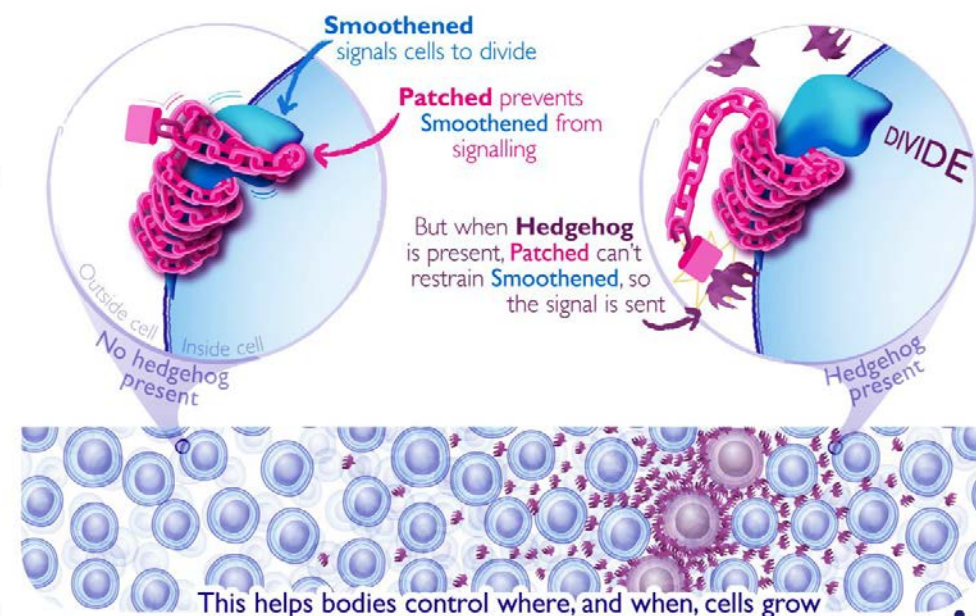
(a)

(b)



(c)

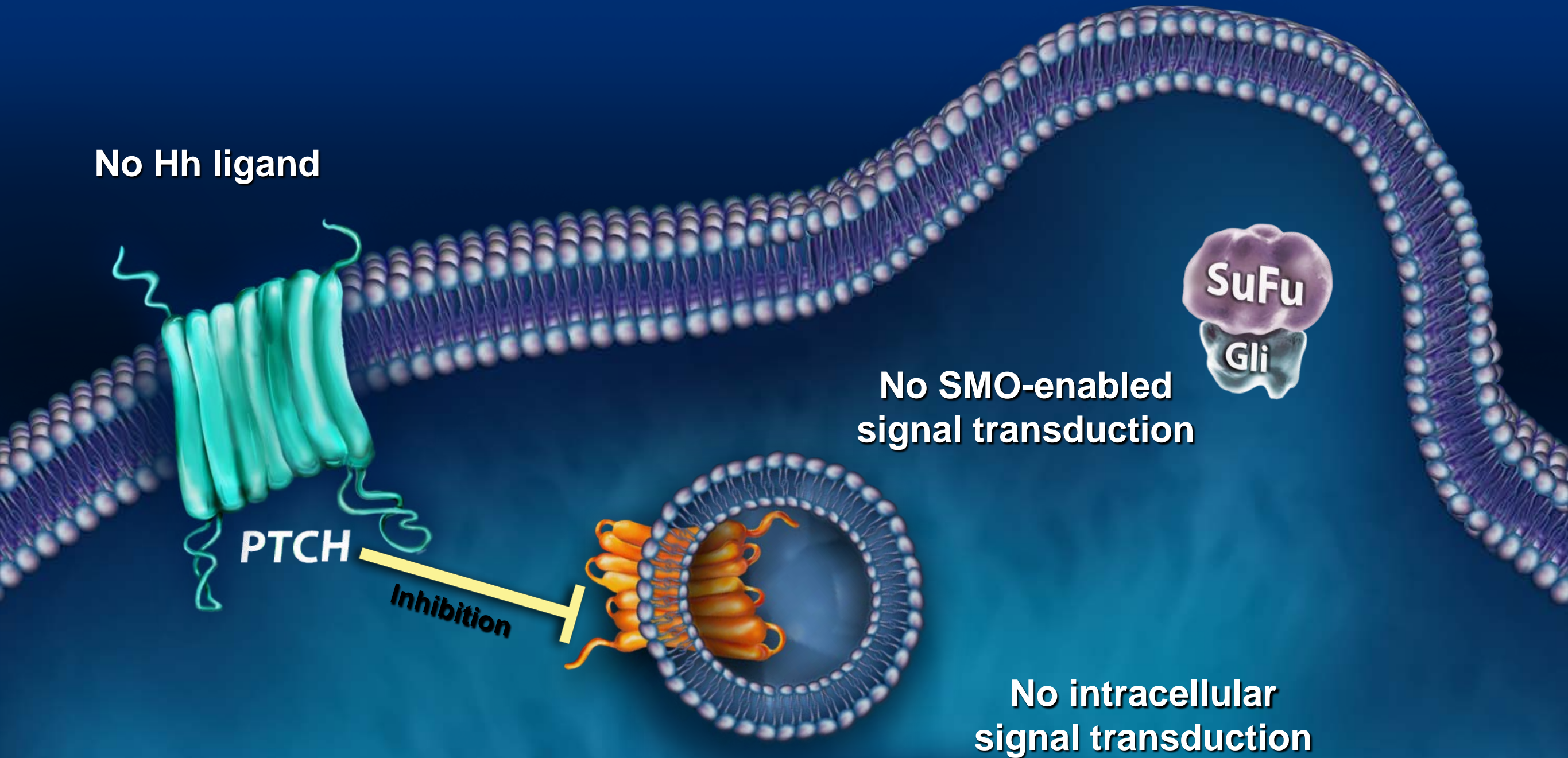
The **hedgehog signalling pathway** controls when and where cells divide.



This helps bodies control where, and when, cells grow

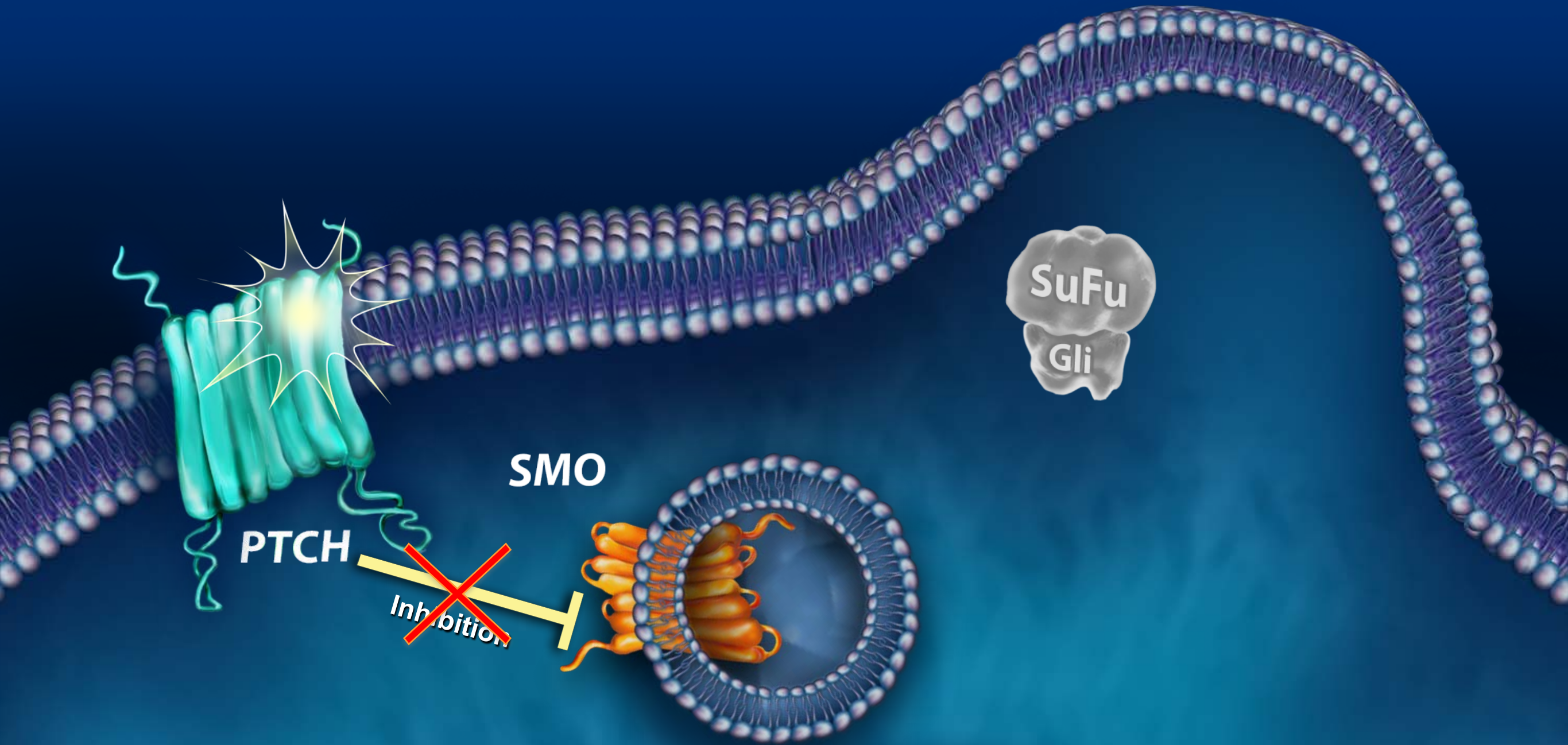
When the Hedgehog pathway is inactive Patched inhibits Smoothened activity

No Hh ligand



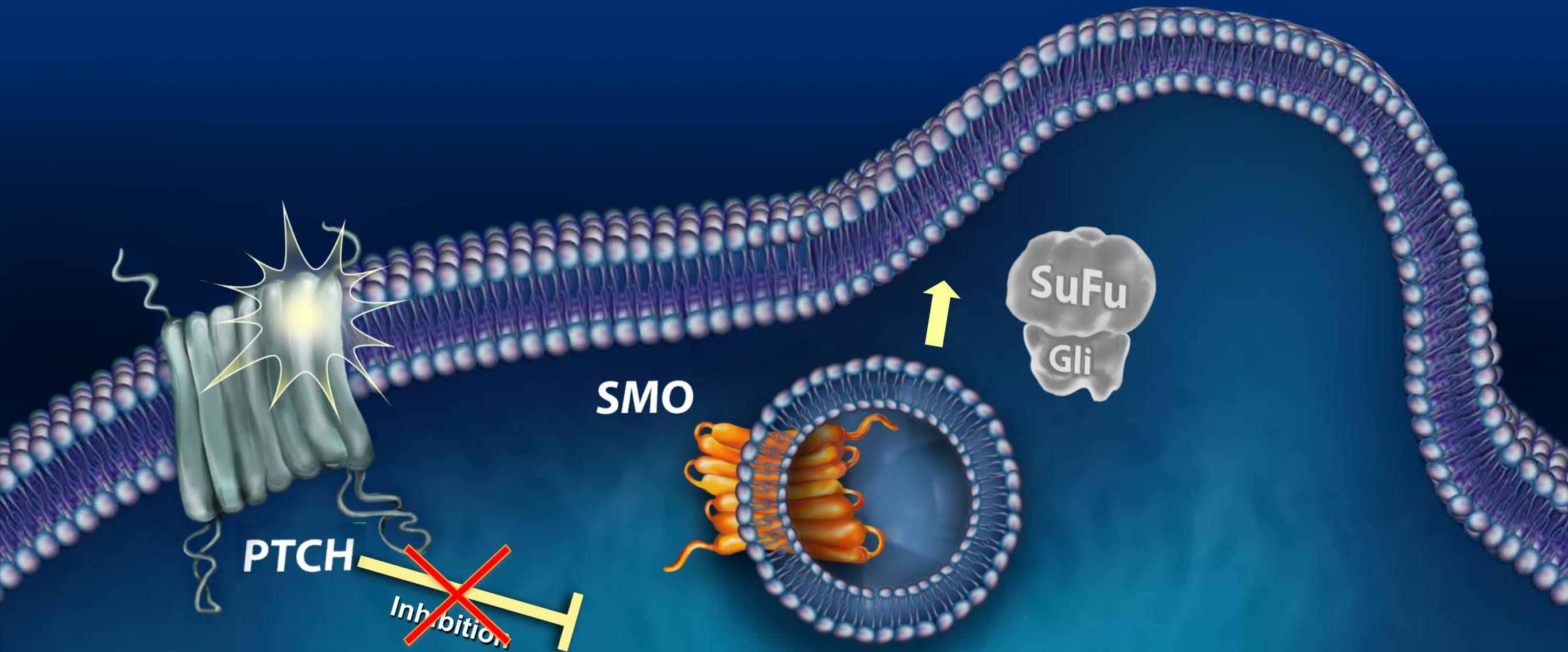
In the absence of Hh ligand, PTCH inhibits SMO and the Hedgehog signalling pathway is suppressed

Mutation-driven Hedgehog signalling is involved in BCC: Inactivating PTCH mutations



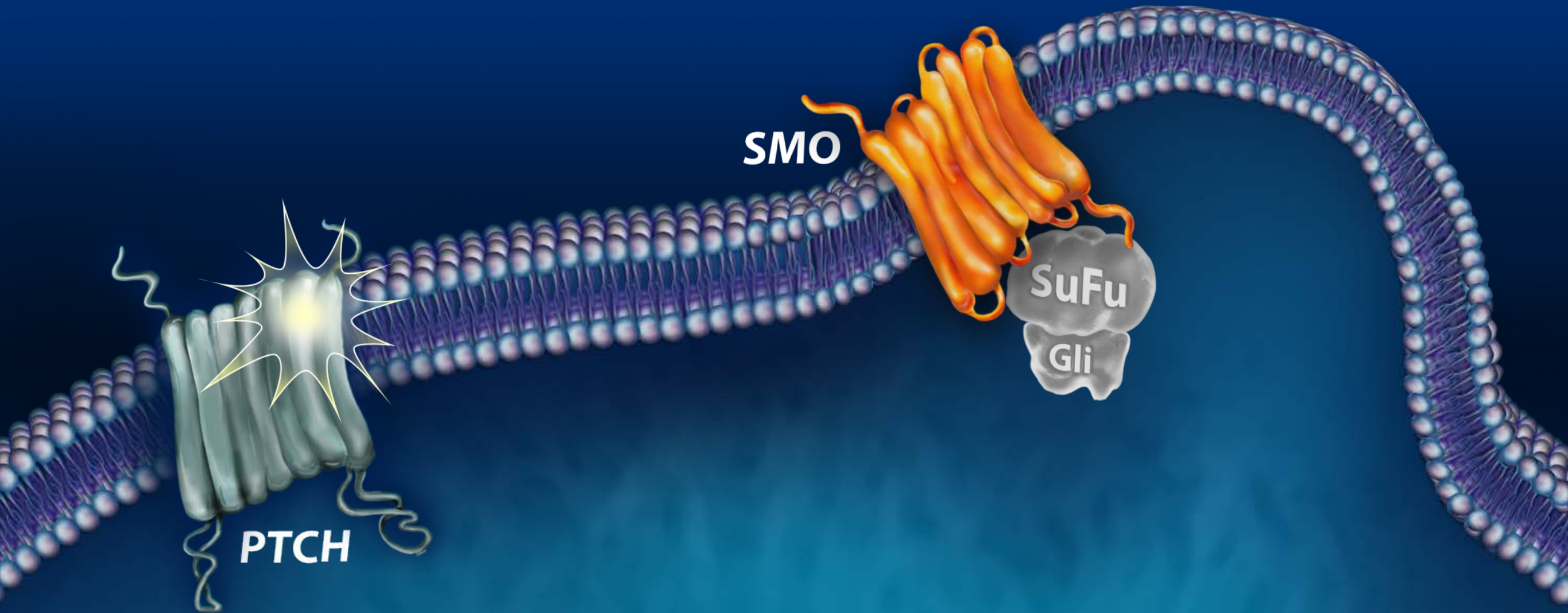
Inactivating mutations of PTCH lead to constitutive pathway activation

Mutation-driven Hedgehog signalling is involved in BCC: Inactivating PTCH mutations



Inactivating mutations of PTCH lead to constitutive pathway activation

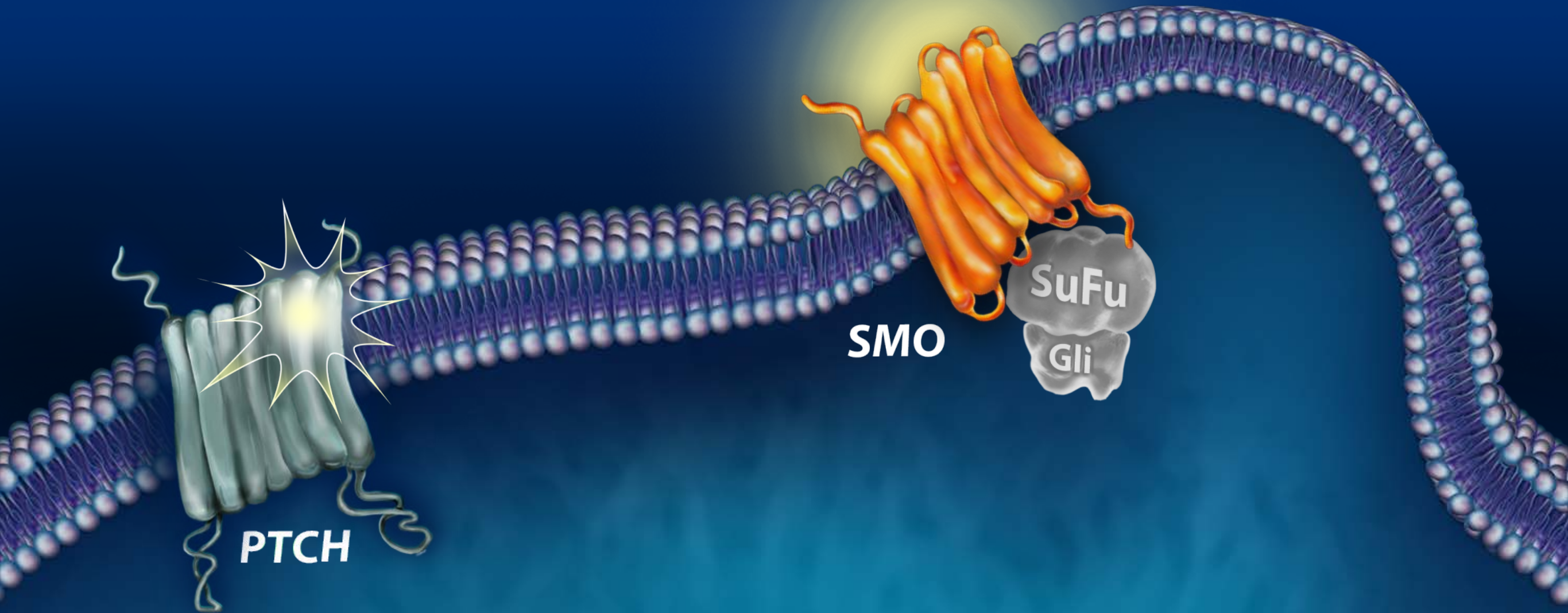
Mutation-driven Hedgehog signalling is involved in BCC: Inactivating PTCH mutations



Inactivating mutations of PTCH lead to constitutive pathway activation



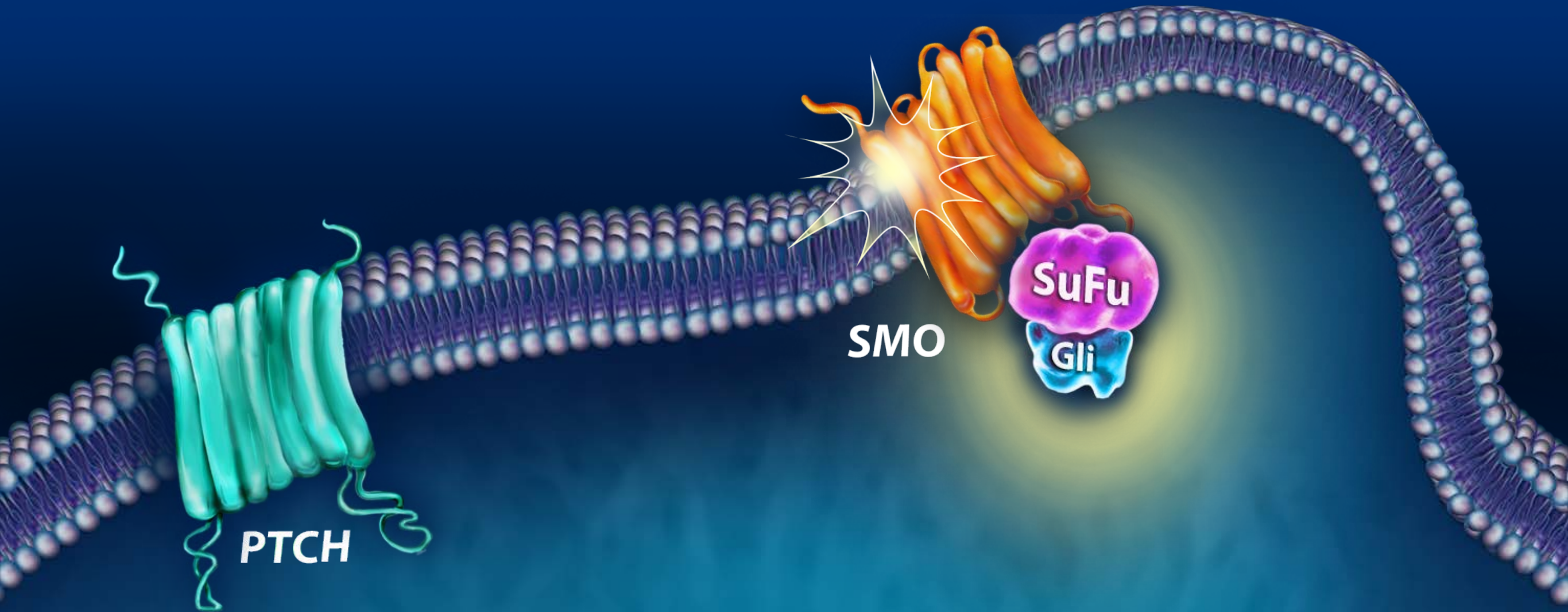
Mutation-driven Hedgehog signalling is involved in BCC: Inactivating PTCH mutations



Inactivating mutations of PTCH lead to constitutive pathway activation



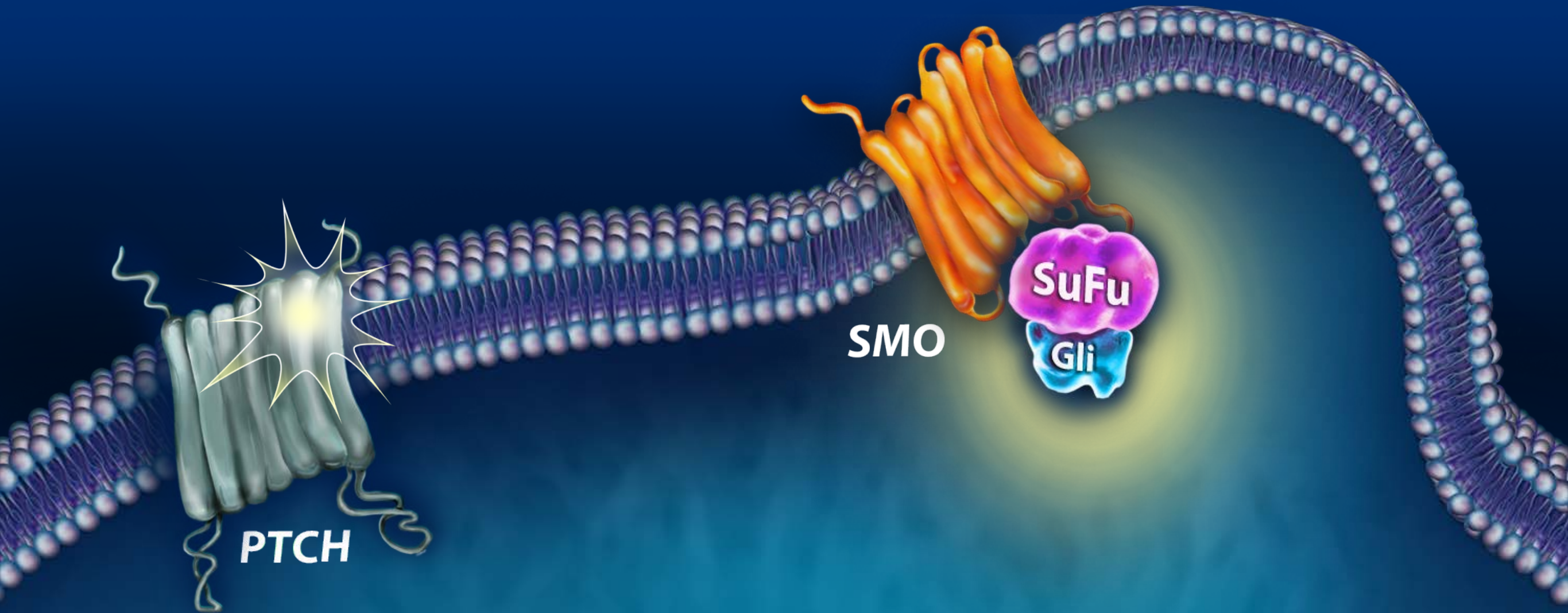
Mutation-driven Hedgehog signalling is involved in BCC: Activating SMO mutations



Activating SMO mutations lead to constitutive pathway activation

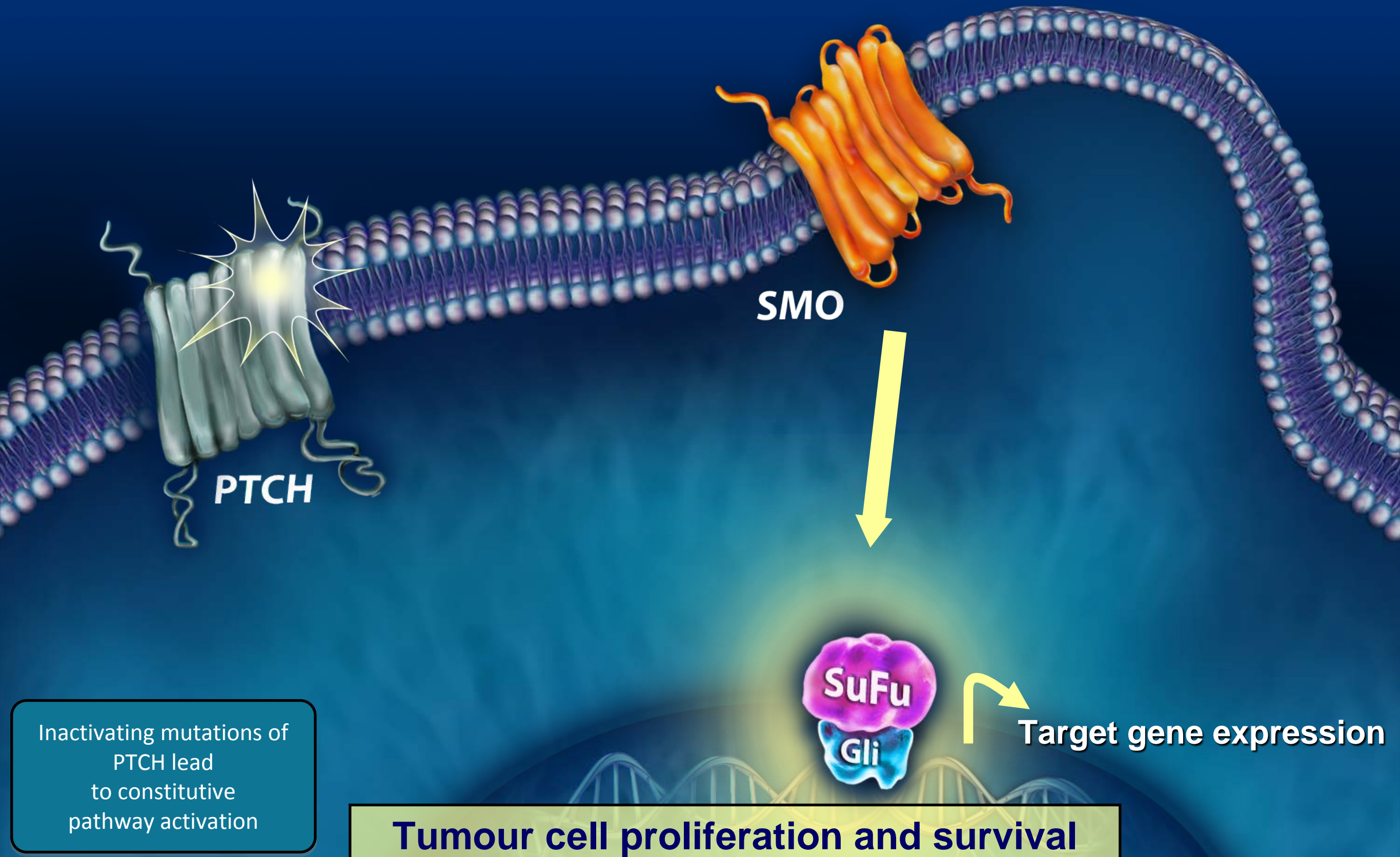


Mutation-driven Hedgehog signalling is involved in BCC: Inactivating PTCH mutations



Inactivating mutations of PTCH lead to constitutive pathway activation

Mutation-driven Hedgehog signalling is involved in BCC: Inactivating PTCH mutations





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journal homepage: www.ejcancer.com



Original Research

Diagnosis and treatment of basal cell carcinoma: European consensus—based interdisciplinary guidelines



Ketty Peris ^{a,b,*}, Maria Concetta Fagnoli ^{c,1}, Claus Garbe ^d,
Roland Kaufmann ^e, Lars Bastholt ^f, Nicole Basset Seguin ^g,
Veronique Bataille ^h, Veronique del Marmol ⁱ, Reinhard Dummer ^j,
Catherine A. Harwood ^k, Axel Hauschild ^l, Christoph Höller ^m,
Merete Haedersdal ⁿ, Josep Malvehy ^o, Mark R. Middleton ^p,
Colin A. Morton ^q, Eduardo Nagore ^r, Alexander J. Stratigos ^s,
Rolf-Markus Szeimies ^t, Luca Tagliaferri ^u, Myrto Trakatelli ^v,
Iris Zalaudek ^w, Alexander Eggermont ^x, Jean Jacques Grob ^y On behalf of
the European Dermatology Forum (EDF), the European Association of
Dermato-Oncology (EADO) and the European Organization for Research
and Treatment of Cancer (EORTC)



1 CPR/DIE AL GIORNO DA 150mg



1 CPR/DIE AL GIORNO DA 200mg

1° CASO

- C.M.
- 76 anni;
- comorbidità: ipertensione, diabete;
- Paziente affetto, da 10 anni, da carcinoma basocellulare pluri-recidivante. Il carcinoma è stato più volte trattato chirurgicamente e radioterapia;







2° CASO

- L.M.
- 84 anni
- Comorbidità: ipertensione arteriosa, fibrillazione atriale

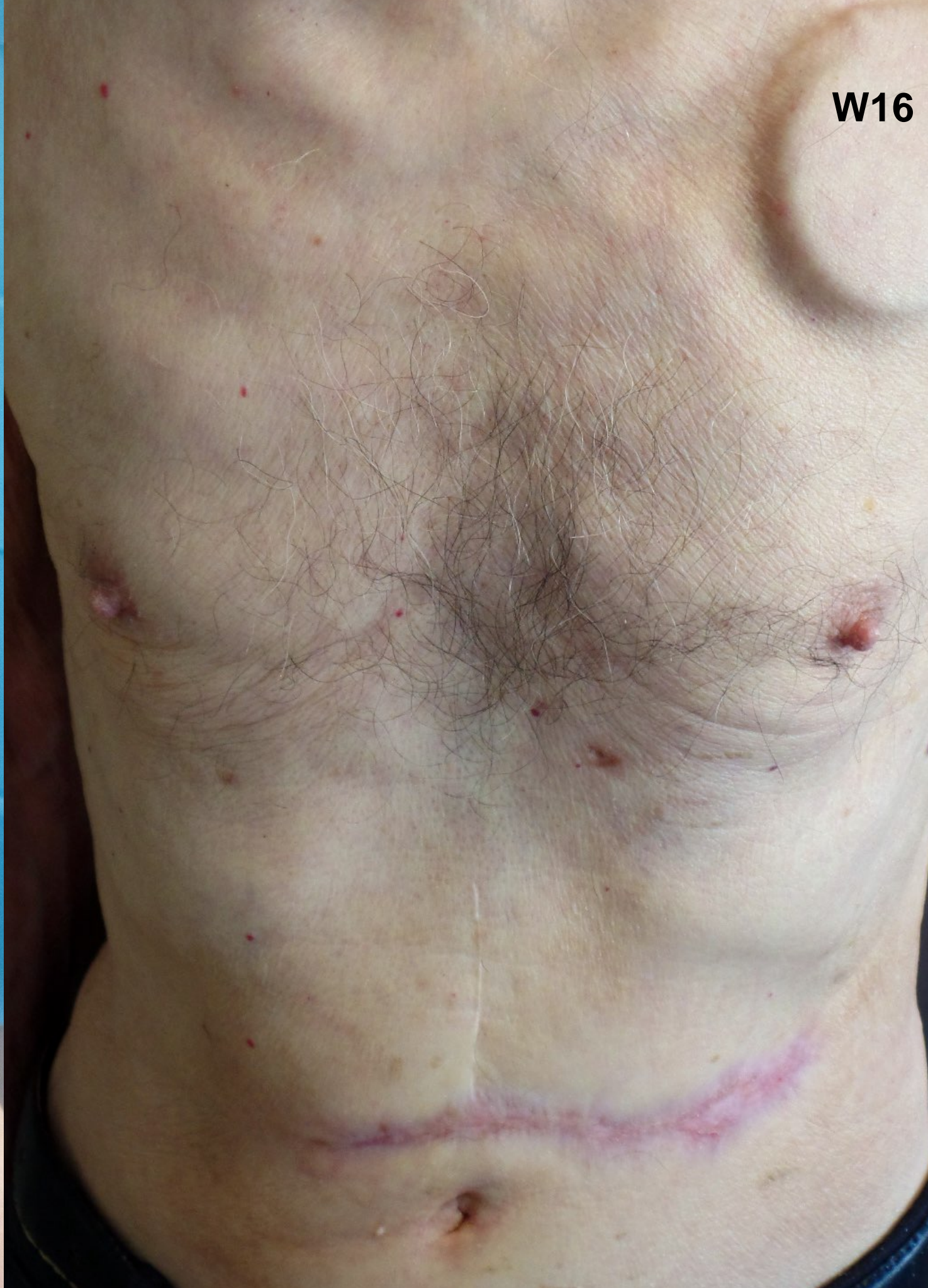




W16



W16



3°CASO

- B.A.
- 69 anni
- Il paziente riferisce l'insorgenza della lesione da circa 10 anni
- Lesione singola; dimensione: ca **3.6 x 3 cm**
- Il paziente ha subito circa **3** interventi di Chirurgia Plastica e **2** cicli di Radioterapia
- Comorbidity: ipertensione in trattamento con diuretici (furosemide)

W0



W16



W20



W24



4 °CASO

- F.V.
- 90 anni
- pregresso infarto miocardico, ipertensione, demenza senile

W0





W16



ORIGINAL PAPER

WILEY

Efficacy and safety of Vismodegib treatment in patients with advanced basal cell carcinoma and multiple comorbidities

Giulia Spallone¹ | Pietro Sollena² | Alessandra Ventura¹ | Maria C. Fagnoli³ |
 Carlota Gutierrez³ | Alfredo Piccerillo² | Sara Tambone³ | Luca Bianchi¹ | Ketty Peris²

TABLE 1 Patients characteristics, duration and treatment outcome after vismodegib therapy

Patient	Age	Sex	BCC lesions	BCC site	Comorbidities	Vismodegib (Tx duration, OR)
1	81	M	Ulcerated BCC (3.5 × 2 cm)	Scalp	Atrial fibrillation, miocardial infarction	6 months CR
2	66	M	Ulcerated BCC (7 × 5 cm)	Scalp	AV valve reconstruction, triple bypass surgery, chronic cardiac deficiency type II diabetes, hypercholesterolemia	6 months CR
3	76	M	Ulcerated BCC (10 × 5 cm) with undefined margins	Face	CKD stage III, HF NYHA II, BMI 37kg/m ²	8 months CR
4	84	F	Ulcerated BCC (3 cm) and multiple BCCs (NBCCS)	Face and trunk	Chronic AF, HF NYHA III, hypertension, difficulties in speaking/eating	8 months CR
5	67	M	Multifocal and Ulcerated BCC (10 × 5 cm) with undefined margins	Scalp	NYHA I, atrioventricular nodal reentry tachycardia, type II diabetes, hypertension	10 months CR
6	83	M	Multiple BCC (>30) and 2 SCC	Trunk	Thrombocytopenia, myeloproliferative disease	6 months PD
7	88	F	laBCC (2 × 1 cm)	Nose	Congestive heart failure, depression, chronic HCV infection	6 months CR
8	93		Ulcerated laBcc (3 × 3 cm)	Nose	Severe dementia, type II diabetes, hyperuricemia	4 months CR

NEL FUTURO?

Review

Understanding the Molecular Genetics of Basal Cell Carcinoma

Cristina Pellegrini [†], Maria Giovanna Maturo [†], Lucia Di Nardo [†], Valeria Ciciarelli, Carlota Gutiérrez García-Rodrigo and Maria Concetta Fargnoli ^{*}

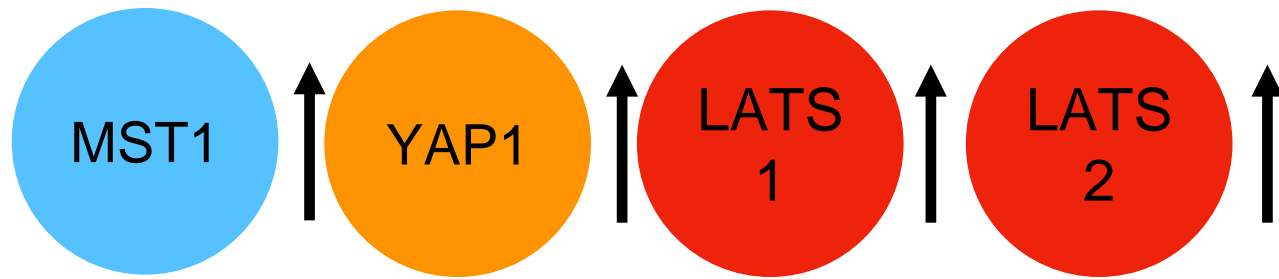
Expression profile of sonic hedgehog signaling-related molecules in basal cell carcinoma

Hye Sung Kim ^{1,☯}, Young Sil Kim ^{1,☯}, Chul Lee ², Myung Soo Shin ³, Jae Wang Kim ⁴, Bo Gun Jang ^{1,*}

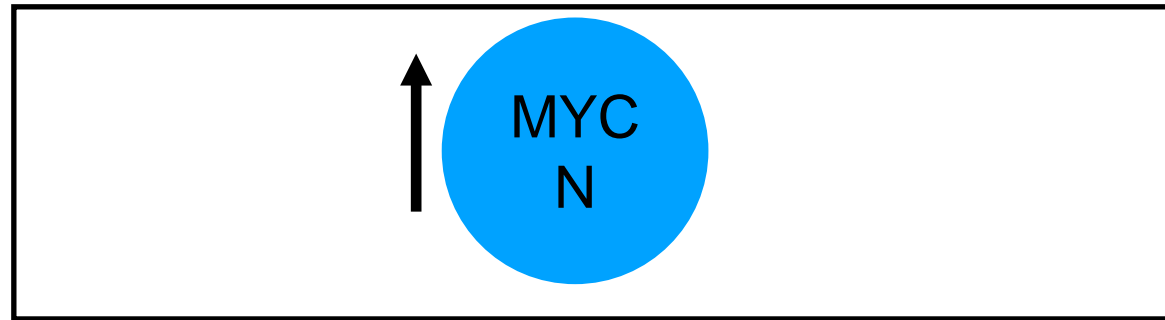
¹ Department of Pathology, Jeju National University College of medicine, Jeju, South Korea, ² Department of Pathology, Seoul National University College of medicine, Seoul, South Korea, ³ Department of Plastic Surgery, Jeju National University College of medicine, Jeju, South Korea, ⁴ Department of Dermatology, Jeju National University College of medicine, Jeju, South Korea

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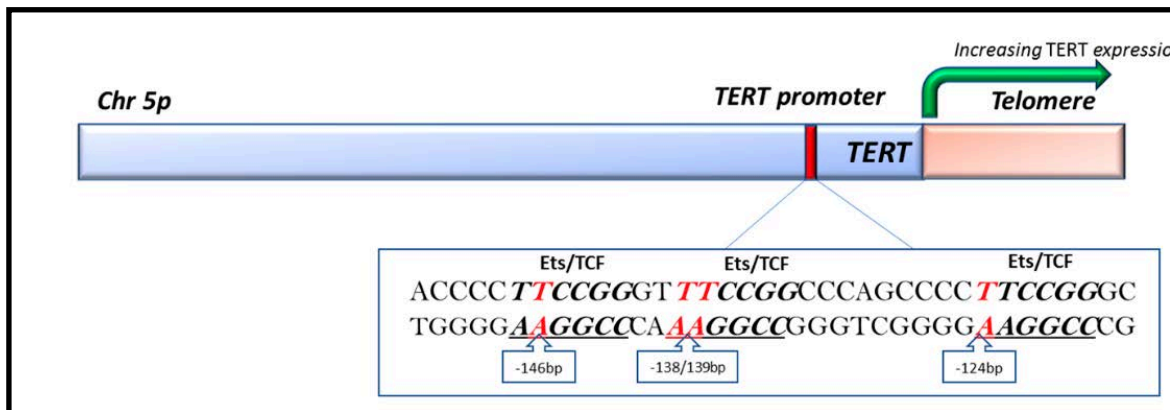
Hippo-YAP Signaling Genes



MYCN/FBXW7 Signaling



TERT Promoter

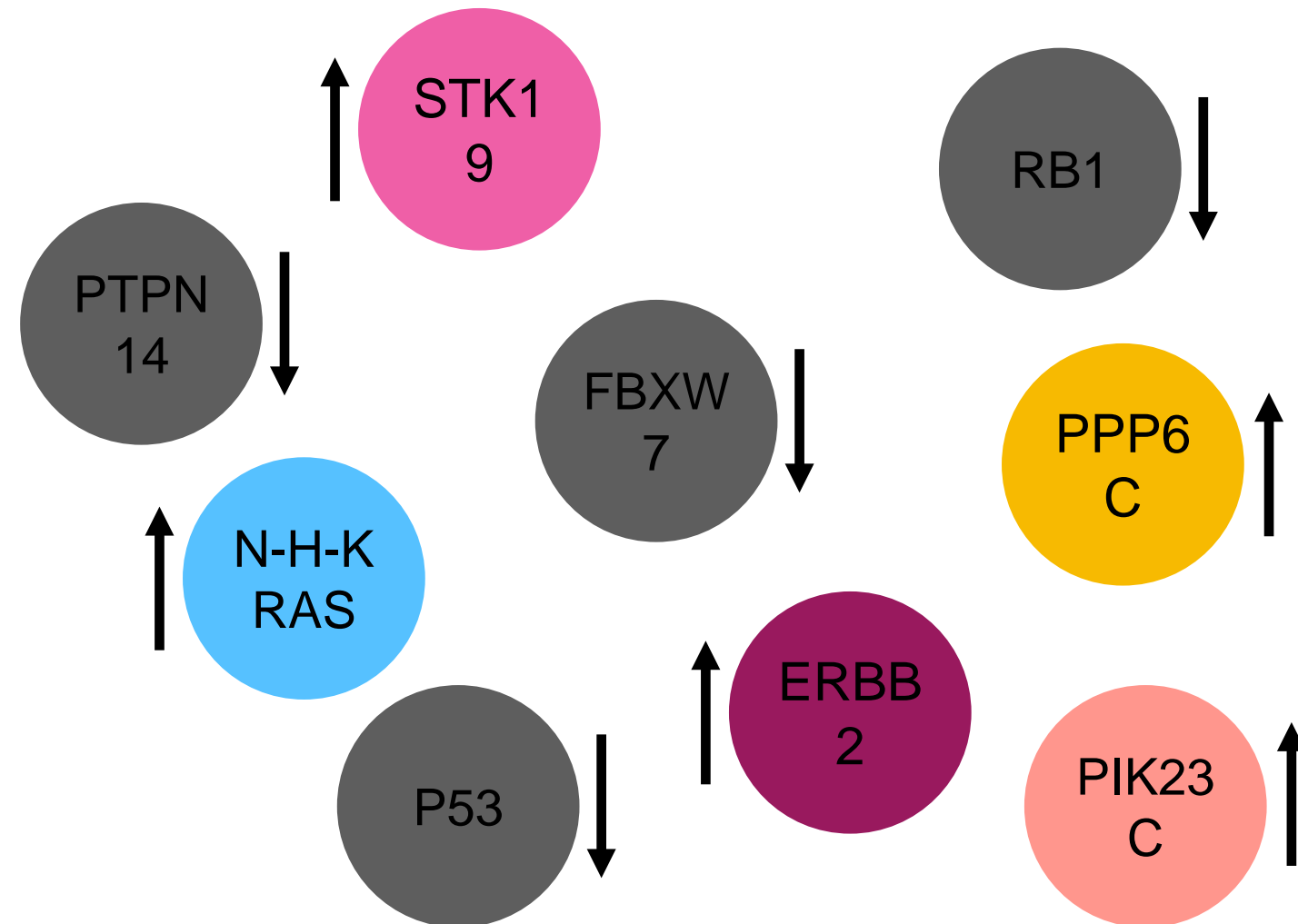


Cancer Cell
Article

CellPress

Genomic Analysis of Smoothed Inhibitor Resistance in Basal Cell Carcinoma

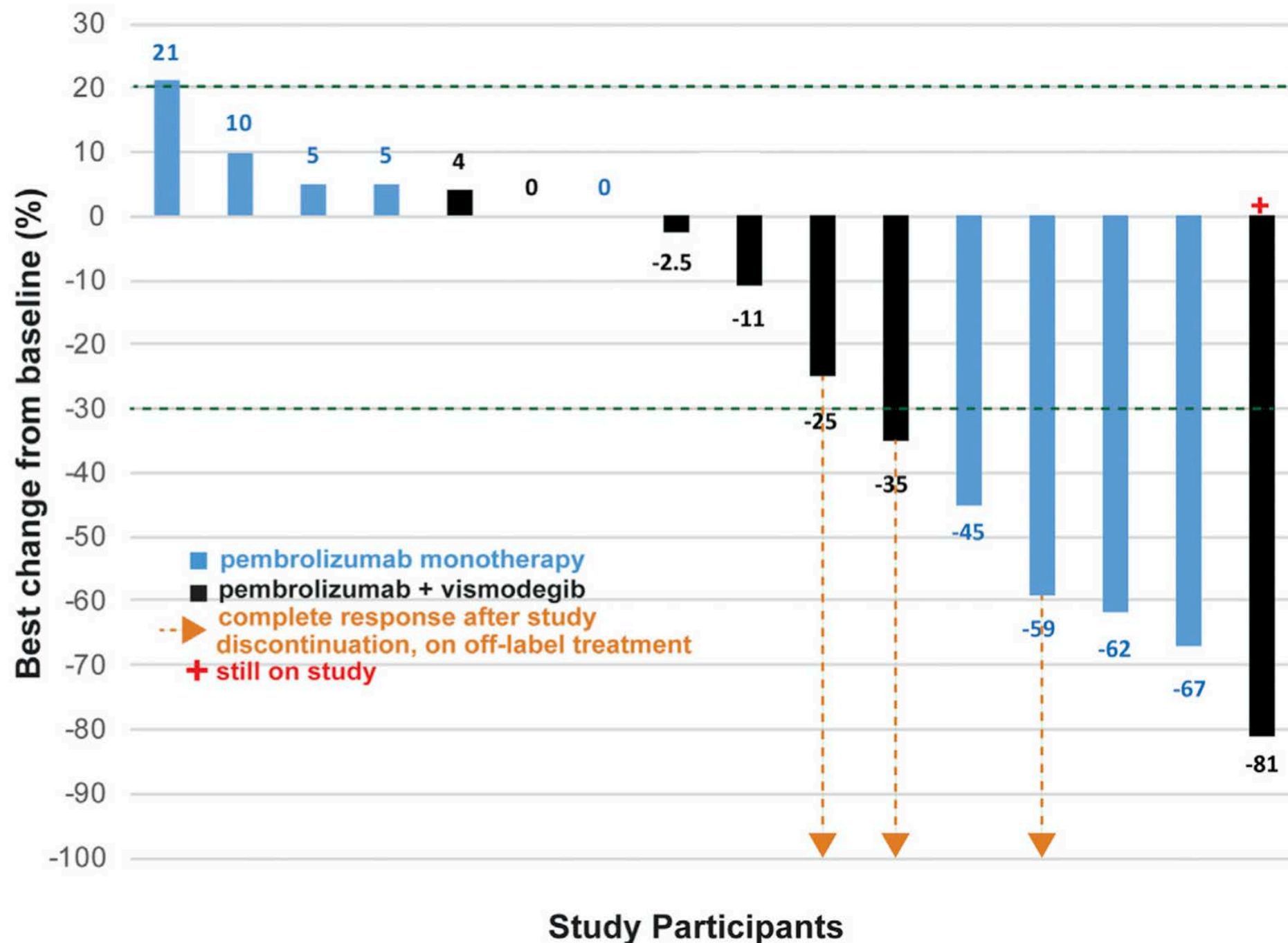
Hayley J. Sharpe,¹ Gregoire Pau,² Gerrit J. Dijkgraaf,¹ Nicole Basset-Seguín,⁵ Zora Modrusan,⁹ Thomas Januario,¹ Vickie Tsui,⁴ Alison B. Durham,⁶ Andrzej A. Dlugosz,⁶ Peter M. Haverly,² Richard Bourgon,² Jean Y. Tang,⁷ Kavita Y. Sarin,⁷ Luc Dirix,⁸ David C. Fisher,⁹ Charles M. Rudin,¹⁰ Howard Sofen,¹¹ Michael R. Migden,¹² Robert L. Yauch,¹ and Frederic J. de Sauvage^{1,*}



	Title	Status	Study Results	Conditions	Interventions	Locations
1	Nivolumab Alone or Plus Ipilimumab for Patients With Locally-Advanced Unresectable or Metastatic Basal Cell Carcinoma	Recruiting	No Results Available	•Basal Cell Carcinoma	•Drug: Nivolumab •Drug: Ipilimumab	•Johns Hopkins Hospital, Baltimore, Maryland, United States
2	Tacrolimus, Nivolumab, and Ipilimumab in Treating Kidney Transplant Recipients With Selected Unresectable or Metastatic Cancers	Recruiting	No Results Available	•Clinical Stage III Cutaneous Melanoma AJCC v8 •Clinical Stage III Merkel Cell Carcinoma AJCC v8 •Clinical Stage IV Cutaneous Melanoma AJCC v8 •Clinical Stage IV Merkel Cell Carcinoma AJCC v8 •High-Frequency Microsatellite Instability •Metastatic Basal Cell Carcinoma •Metastatic Melanoma •Metastatic Merkel Cell Carcinoma •Metastatic Skin Squamous Cell Carcinoma •Pathologic Stage III Cutaneous Melanoma AJCC v8 •and 12 more	•Biological: Ipilimumab •Biological: Nivolumab •Drug: Prednisone •Drug: Tacrolimus	•Johns Hopkins University/Sidney Kimmel Cancer Center, Baltimore, Maryland, United States •University of Pittsburgh Cancer Institute (UPCI), Pittsburgh, Pennsylvania, United States
3	Talimogene Laherparepvec and Nivolumab in Treating Patients With Refractory Lymphomas or Advanced or Refractory Non-melanoma Skin Cancers	Suspended	No Results Available	•Adenoid Cystic Carcinoma •Adnexal Carcinoma •Apocrine Carcinoma •Eccrine Porocarcinoma •Extraocular Cutaneous Sebaceous Carcinoma •Hidradenocarcinoma •Keratoacanthoma •Malignant Sweat Gland Neoplasm •Merkel Cell Carcinoma •Microcystic Adnexal Carcinoma •and 21 more	•Other: Laboratory Biomarker Analysis •Biological: Nivolumab •Biological: Talimogene Laherparepvec	•Los Angeles County-USC Medical Center, Los Angeles, California, United States •USC / Norris Comprehensive Cancer Center, Los Angeles, California, United States •University of California Davis Comprehensive Cancer Center, Sacramento, California, United States •University of Colorado Hospital, Aurora, Colorado, United States •Northwestern University, Chicago, Illinois, United States •University of Kansas Clinical Research Center, Fairway, Kansas, United States •Johns Hopkins University/Sidney Kimmel Cancer Center, Baltimore, Maryland, United States •Massachusetts General Hospital Cancer Center, Boston, Massachusetts, United States •Dana-Farber Cancer Institute, Boston, Massachusetts, United States •Siteman Cancer Center at West County Hospital, Creve Coeur, Missouri, United States
4	Nivolumab and Ipilimumab in Treating Patients With Rare Tumors	Suspended	No Results Available	•Acinar Cell Carcinoma •Adenoid Cystic Carcinoma •Adrenal Cortex Carcinoma •Adrenal Gland Pheochromocytoma •Anal Canal Neuroendocrine Carcinoma •Anal Canal Undifferentiated Carcinoma •Angiosarcoma •Apocrine Neoplasm •Appendix Mucinous Adenocarcinoma •Bartholin Gland Transitional Cell Carcinoma •and 85 more	•Procedure: Biospecimen Collection •Biological: Ipilimumab •Biological: Nivolumab	•University of Alabama at Birmingham Cancer Center, Birmingham, Alabama, United States •University of South Alabama Mitchell Cancer Institute, Mobile, Alabama, United States •Anchorage Associates in Radiation Medicine, Anchorage, Alaska, United States •Anchorage Radiation Therapy Center, Anchorage, Alaska, United States •Alaska Breast Care and Surgery LLC, Anchorage, Alaska, United States •Alaska Oncology and Hematology LLC, Anchorage, Alaska, United States •Alaska Women's Cancer Care, Anchorage, Alaska, United States •Anchorage Oncology Centre, Anchorage, Alaska, United States •Katmai Oncology Group, Anchorage, Alaska, United States •Providence Alaska Medical Center, Anchorage, Alaska, United States •and 910 more
6	Pembrolizumab With or Without Vismodegib in Treating Metastatic or Unresectable Basal Cell Skin Cancer	Completed	Has Results	•Skin Basal Cell Carcinoma	•Biological: Pembrolizumab •Drug: Vismodegib	•Stanford University School of Medicine, Palo Alto, California, United States
10	Pilot Study of Sonidegib and Buparlisib in Treating Patients With Advanced or Metastatic Basal Cell Carcinoma	Terminated	Has Results	•Carcinoma, Basal Cell •Recurrent Skin Cancer •Skin Neoplasms •Basal Cell Nevus Syndrome	•Drug: Buparlisib •Drug: Sonidegib	•Stanford University School of Medicine, Stanford, California, United States

Pembrolizumab for advanced basal cell carcinoma: An investigator-initiated, proof-of-concept study

Anne Lynn S. Chang, MD^a, Duy C. Tran, BS^a, John G. D. Cannon, BS^a, Shufeng Li, MS^a, Mark Jeng, PhD^a, Roma Patel, PA-C^b, Lindsay Van der Bokke, RN^b, Alana Pague, BS^b, Richard Brotherton, RN^b, Kerri E. Rieger, MD PhD^c, Ansuman T. Satpathy, MD, PhD^d, Kathryn E. Yost, BS^d, Sunil Reddy, MD^e, Kavita Sarin, MD, PhD^a, A. Dimitrios Colevas, MD^e



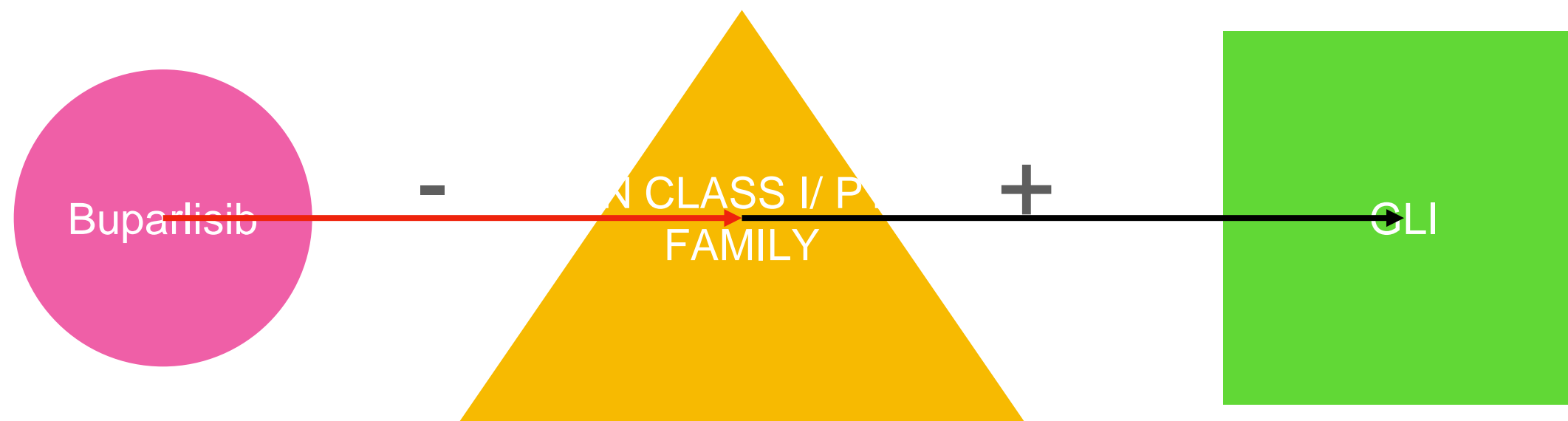
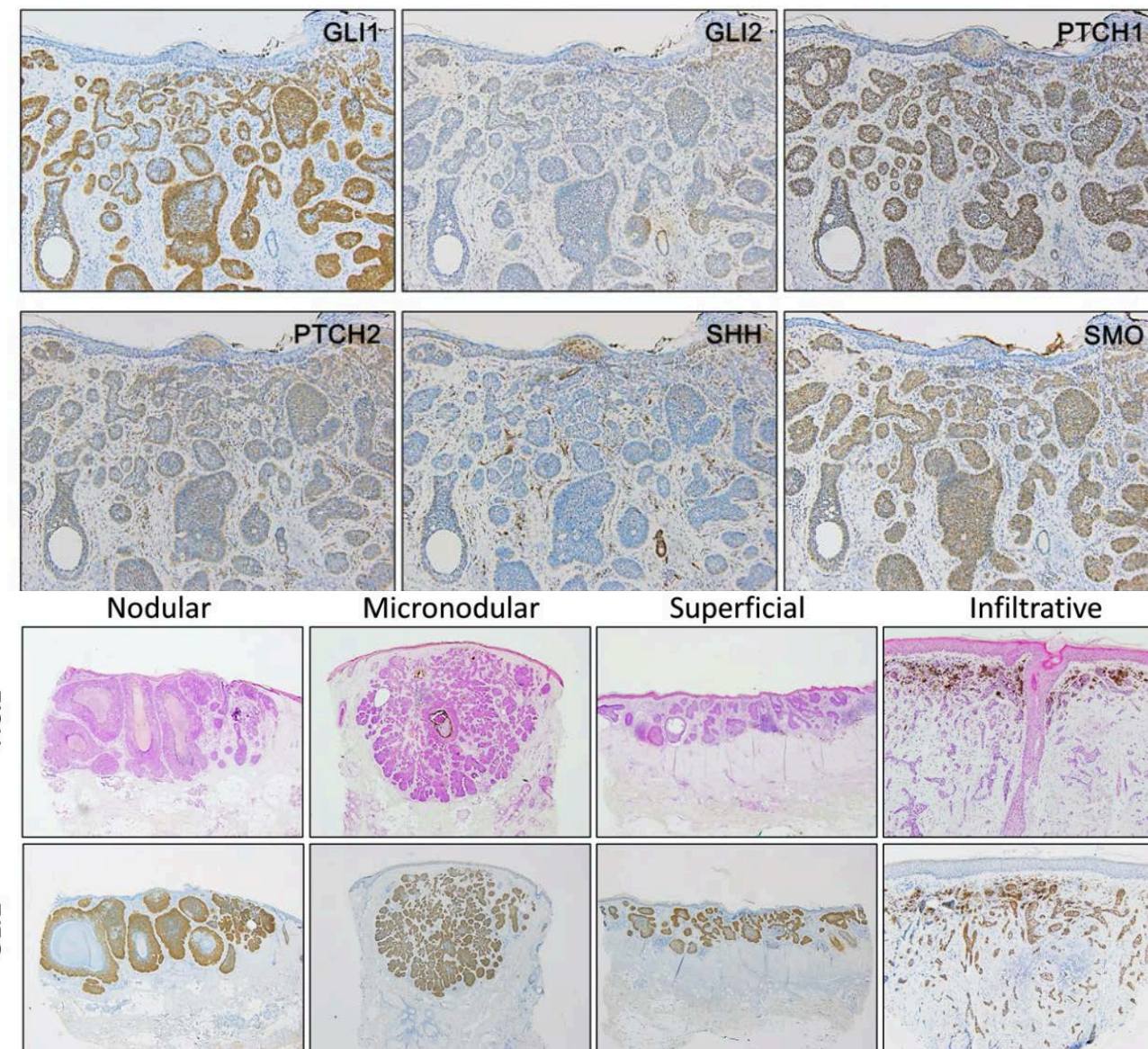
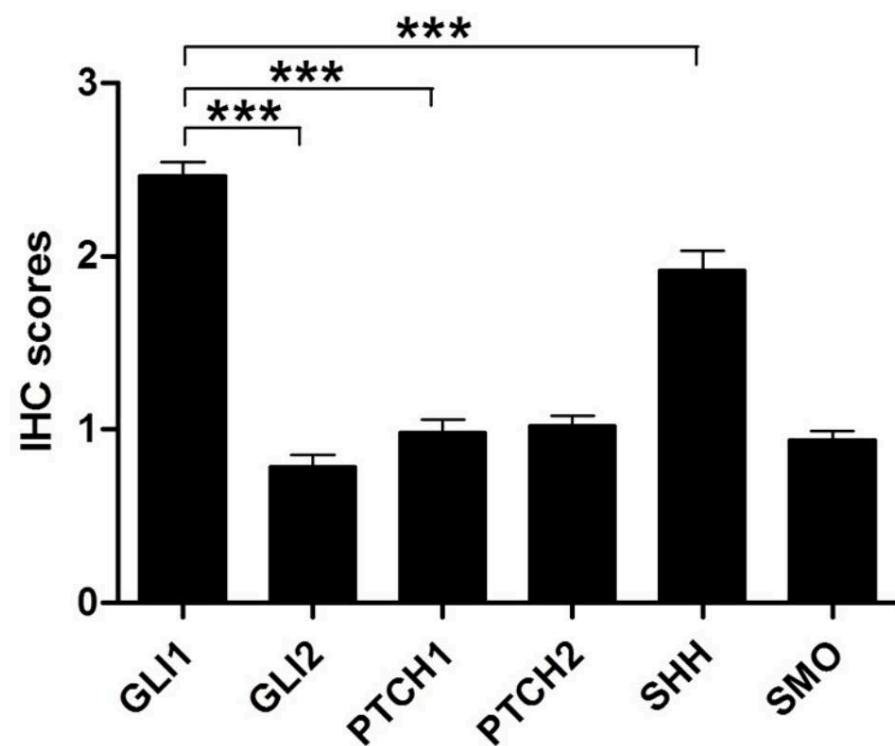
Expression profile of sonic hedgehog signaling-related molecules in basal cell carcinoma

Hye Sung Kim¹*, Young Sil Kim¹*, Chul Lee², Myung Soo Shin³, Jae Wang Kim⁴, Bo Gun Jang¹*



1 Department of Pathology, Jeju National University College of medicine, Jeju, South Korea, **2** Department of Pathology, Seoul National University College of medicine, Seoul, South Korea, **3** Department of Plastic Surgery, Jeju National University College of medicine, Jeju, South Korea, **4** Department of Dermatology, Jeju National University College of medicine, Jeju, South Korea

* These authors contributed equally to this work.

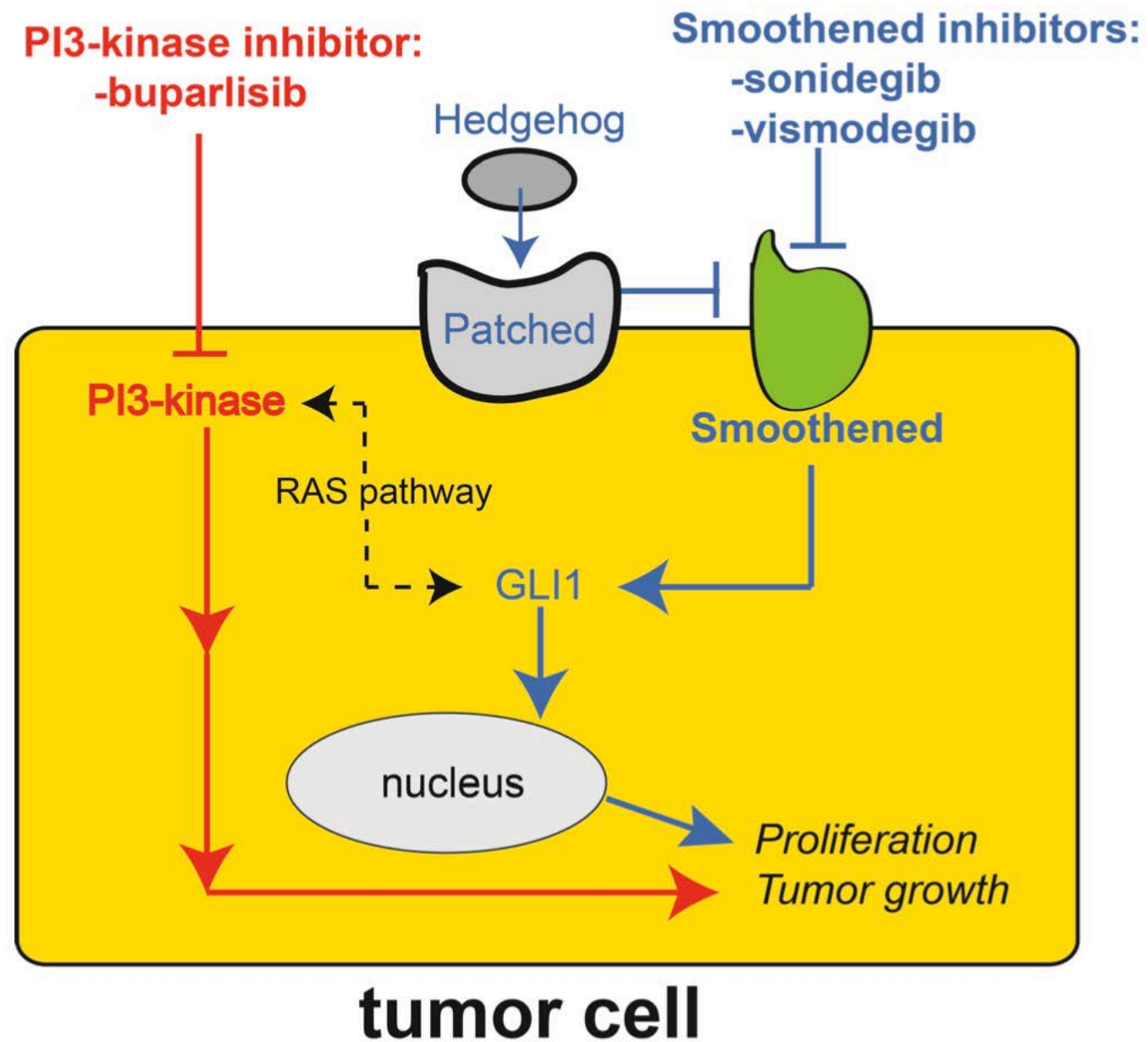
* Bgjang9633@gmail.com



An exploratory open-label, investigator-initiated study to evaluate the efficacy and safety of combination sonidegib and buparlisib for advanced basal cell carcinomas

[Duy Cong Tran](#), BS, [Ann Moffat](#), BA, [Richard Brotherton](#), RN, [Alana Pague](#), BS, [Gefei Alex Zhu](#), MD, [Anne Lynn S. Chang](#), MD*,  

Department of Dermatology, Stanford University School of Medicine, Redwood City, California



GRAZIE

