







neuroendocrine secondaire

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Carrefour Pathologie 2020

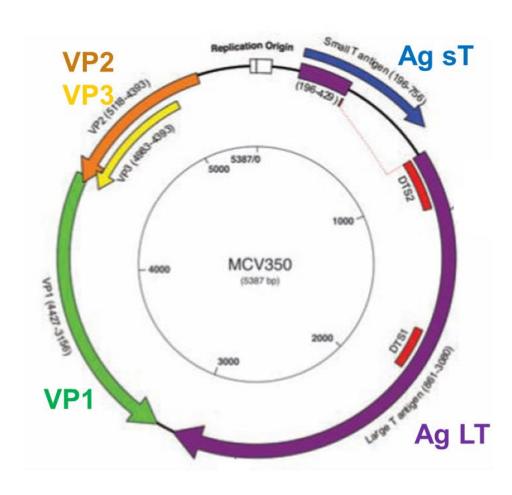
Carcinome à cellules de Merkel

- Incidence : 1/100 000
- Sujet âgé caucasien
- Facteurs de risque :
 - exposition solaire
 - immunodépression
- Survie à 5 ans 40%



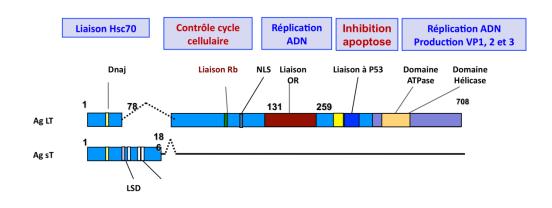


Merkel cell polyomavirus : virologie



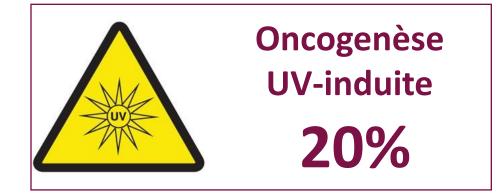


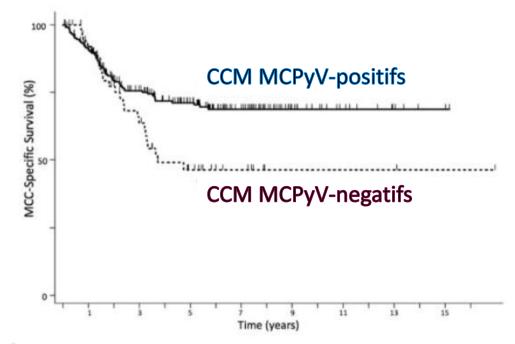




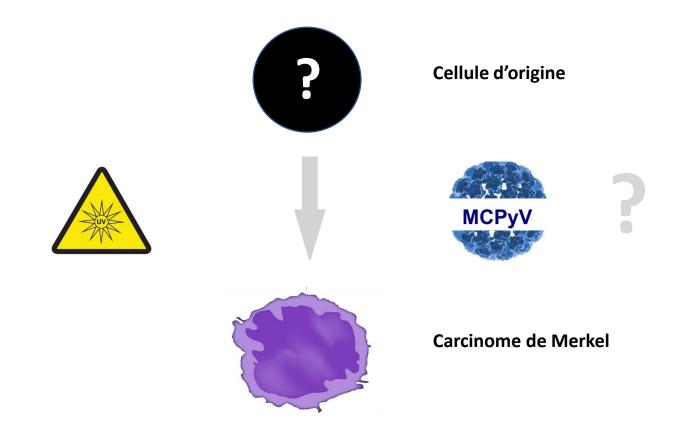
Carcinome de Merkel : étiologie





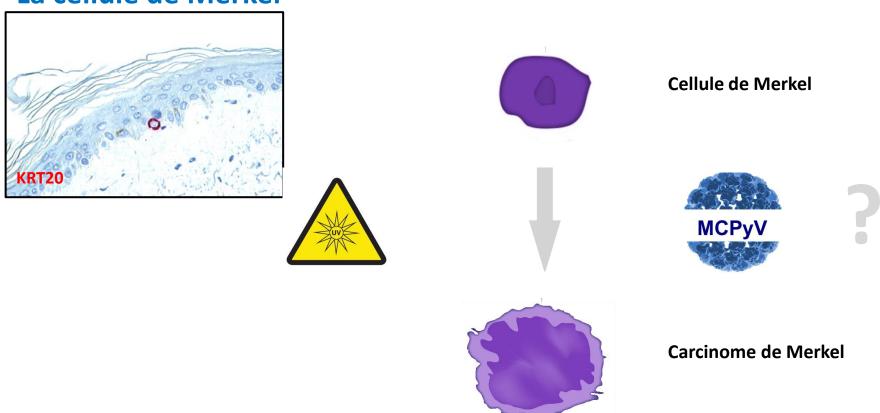


Carcinome de Merkel : cellule d'origine

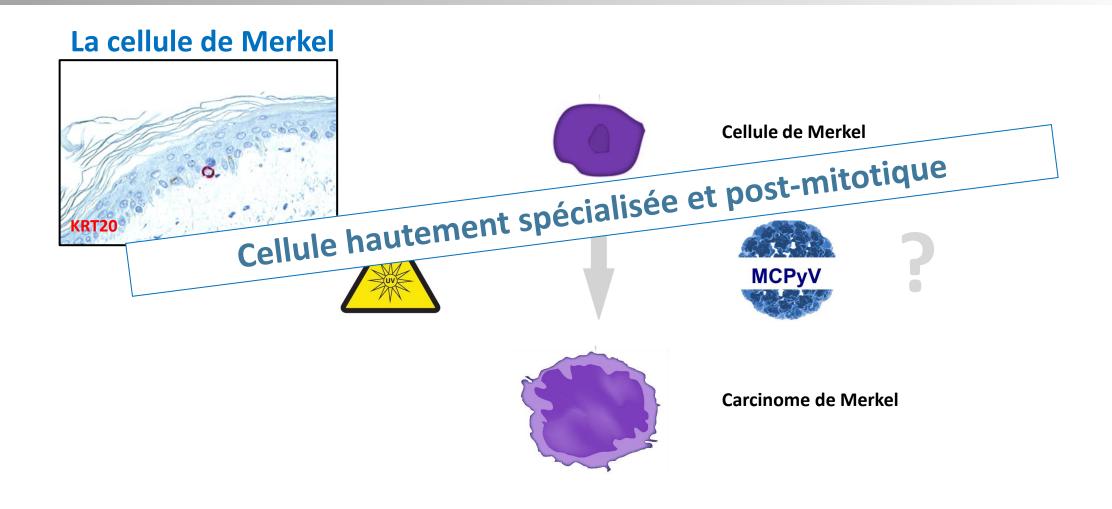


Carcinome de Merkel : cellule d'origine

La cellule de Merkel

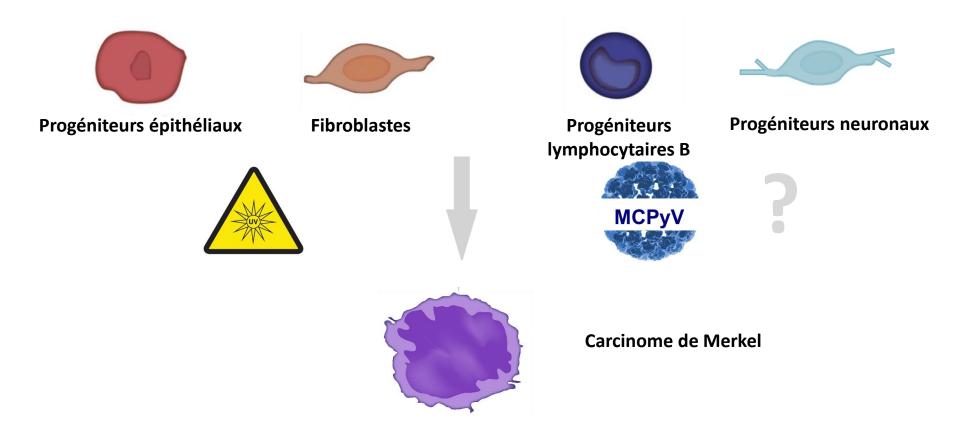


Carcinome de Merkel: cellule d'origine

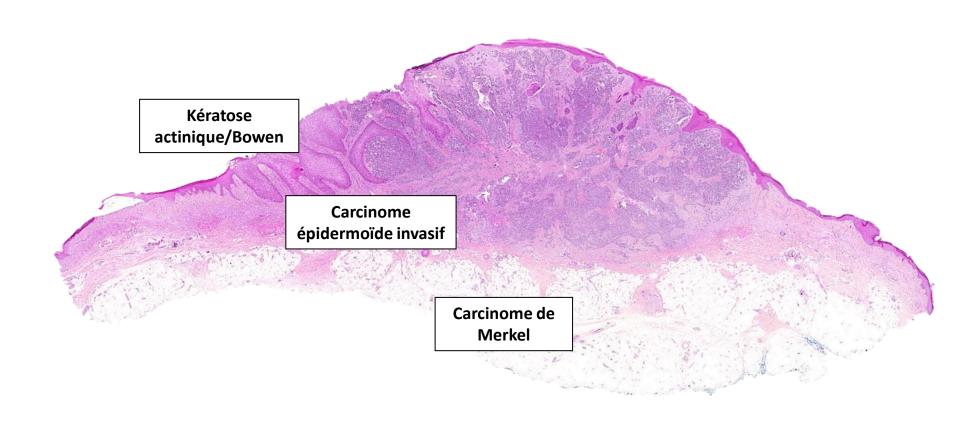


Carcinome de Merkel : cellule d'origine

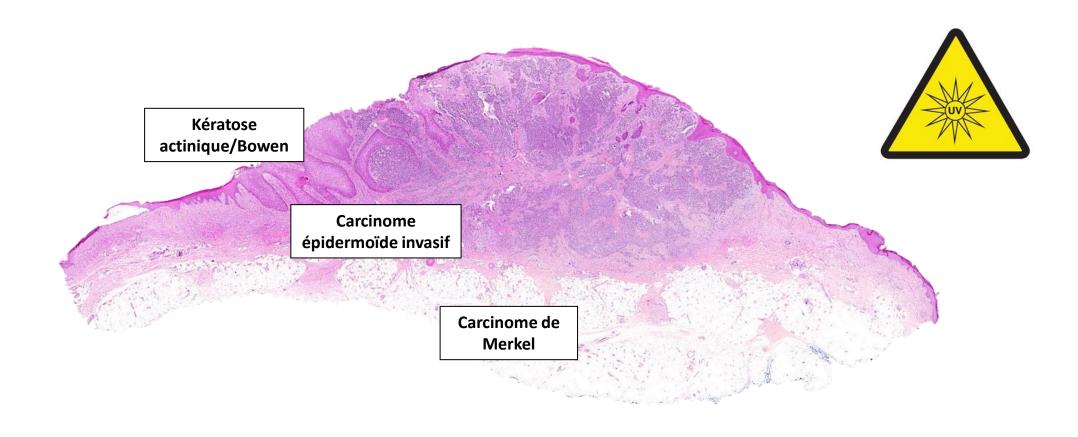
Autres candidats potentiels



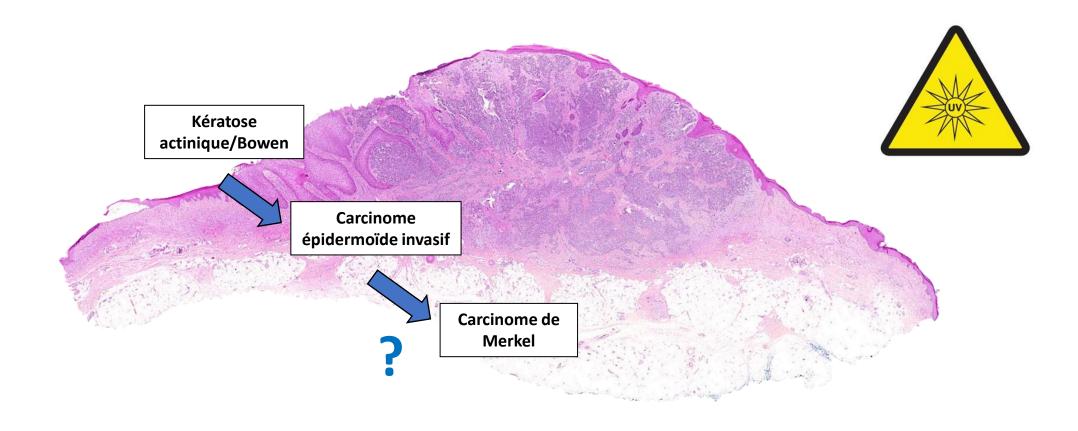
Carcinome de Merkel composite



Carcinome de Merkel composite



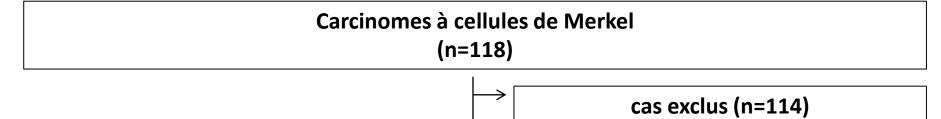
Carcinome de Merkel composite



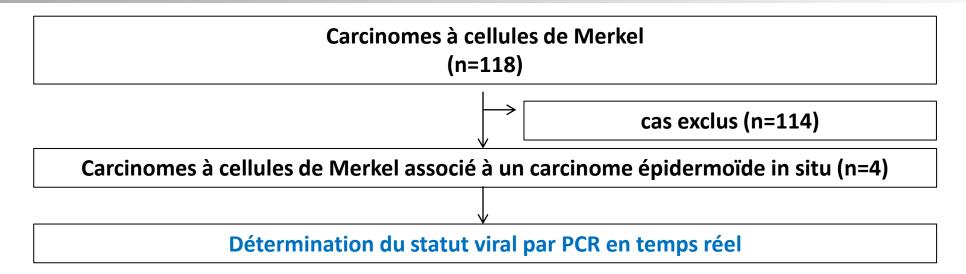
Les tumeurs composites : un témoin de l'histogenèse des CCM-MCPyV(-)?

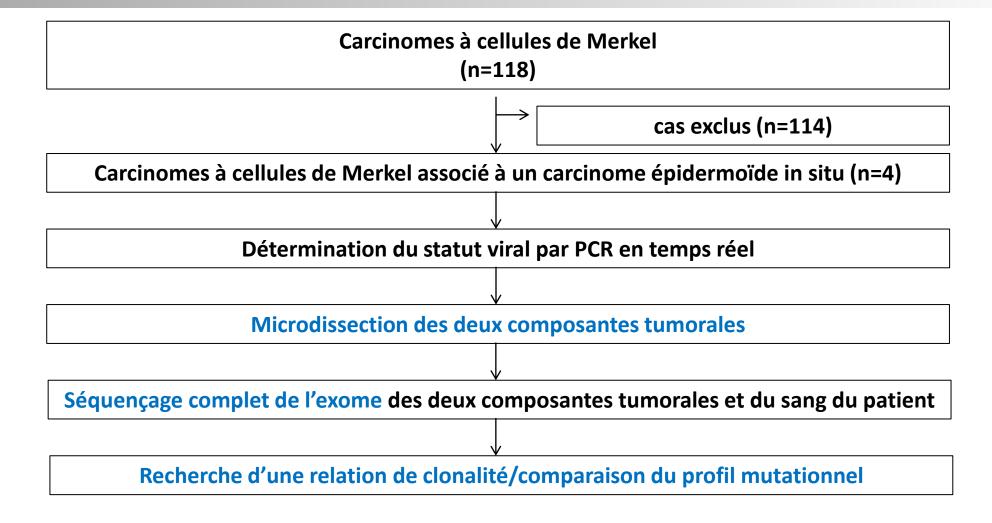
Objectif

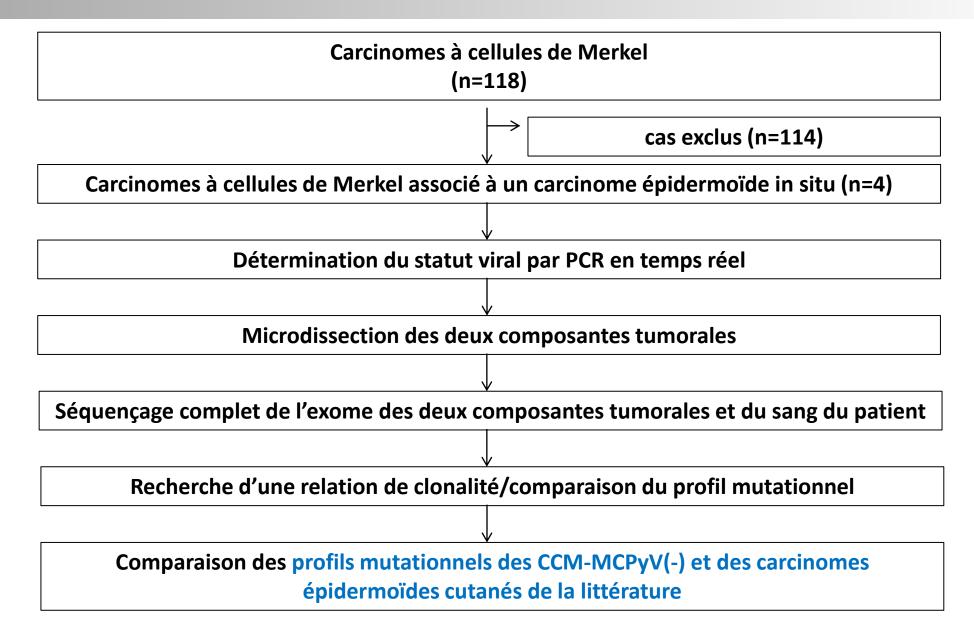
Objectif principal: identifier la cellule d'origine et les mécanismes de développement des CCM- vironégatifs par l'étude de ces tumeurs composites.



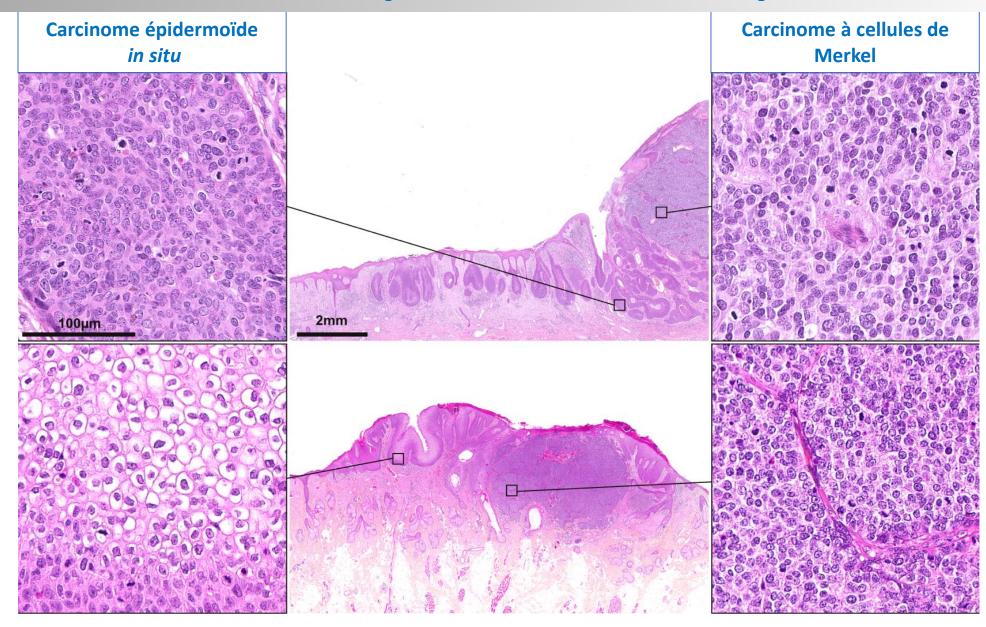
Carcinomes à cellules de Merkel associé à un carcinome épidermoïde in situ (n=4)



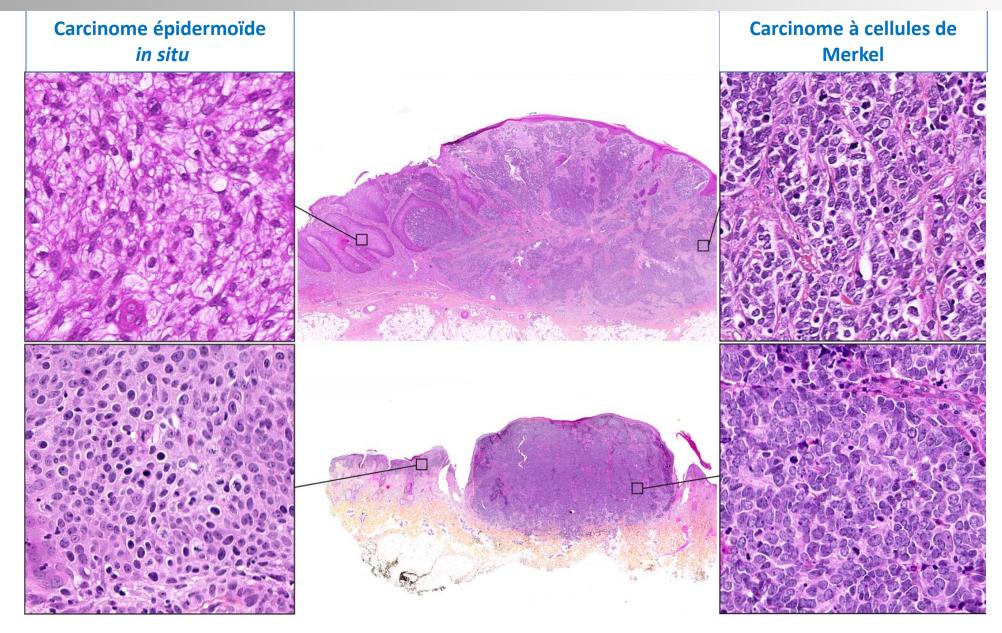




CCM composite: microscopie



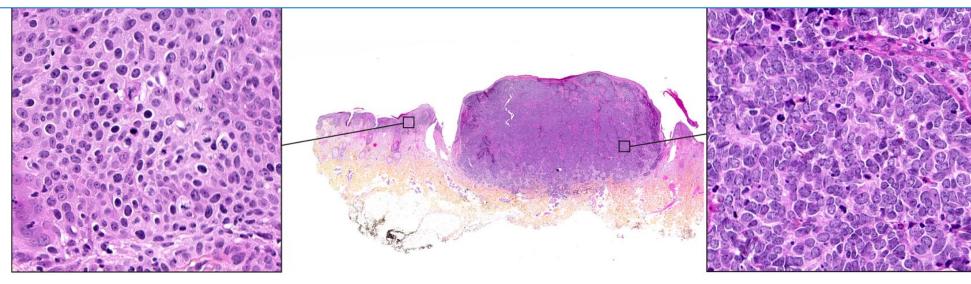
CCM composite : microscopie

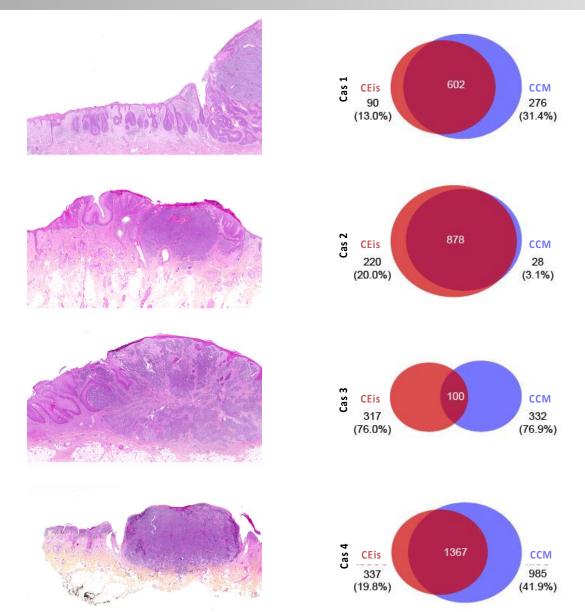


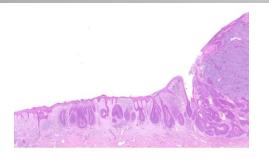
CCM composite: microscopie

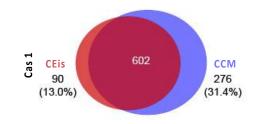


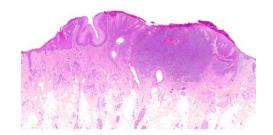
Absence de MCPyV (PCR quantitative)

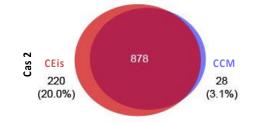








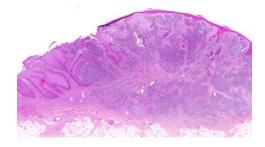


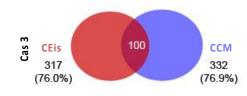




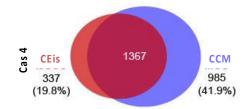


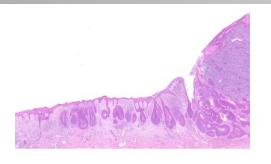


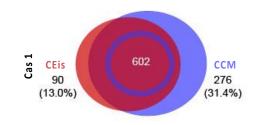


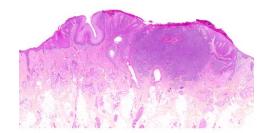


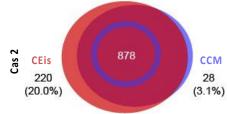








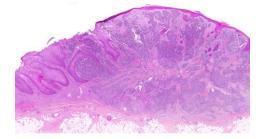


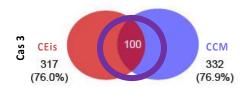










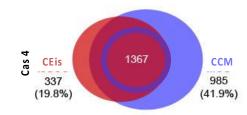


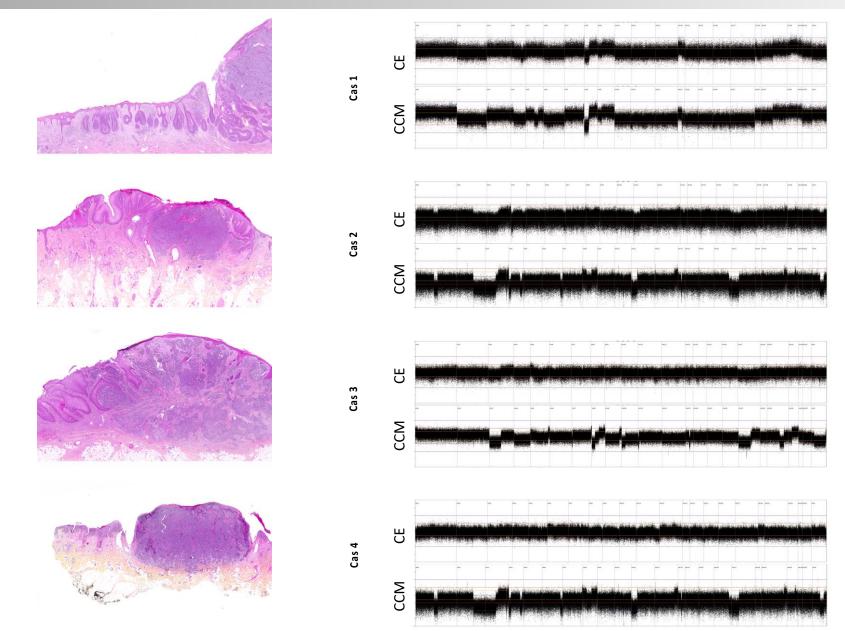
Mutations communes

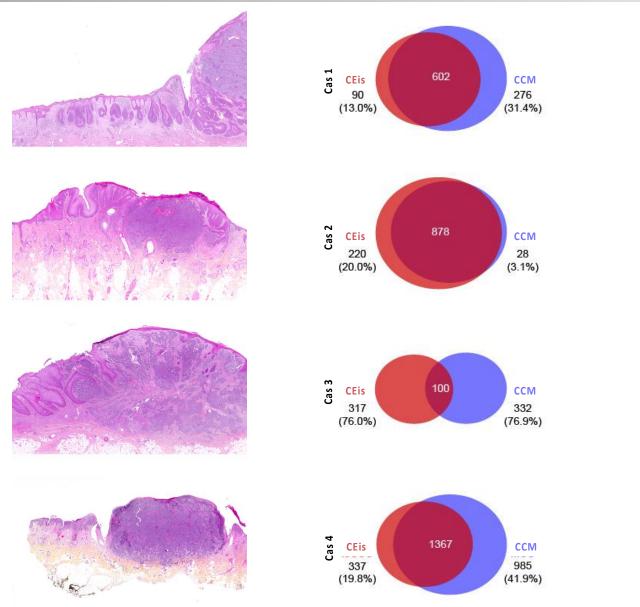
Signature UV

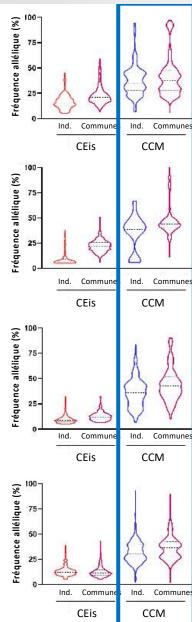
⇒ Preuve de la relation clonale





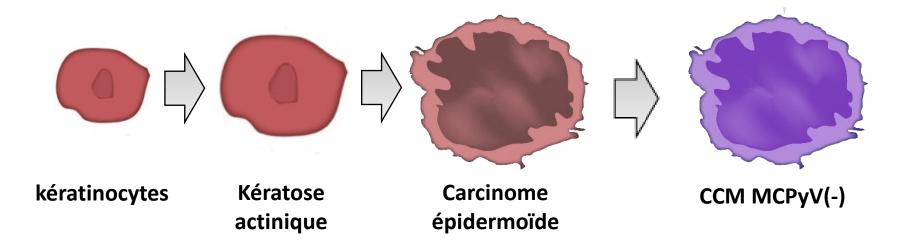






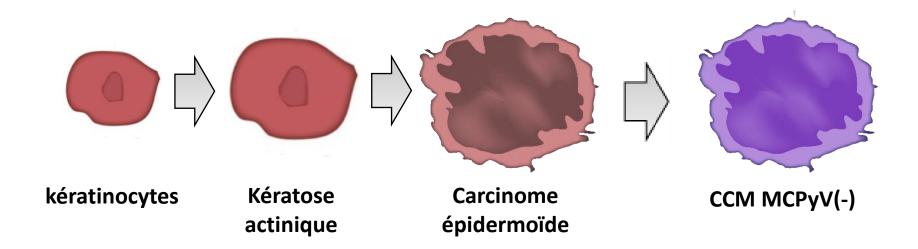
Altérations génétiques

UV



Altérations génétiques

UV

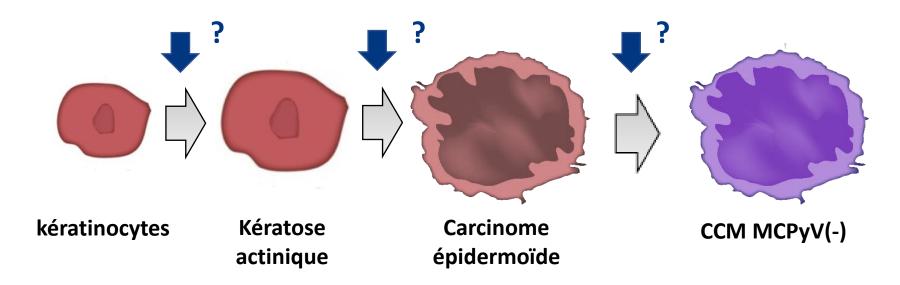


⇒ Preuve de l'origine kératinocytaire des CCM MCPyV(-)



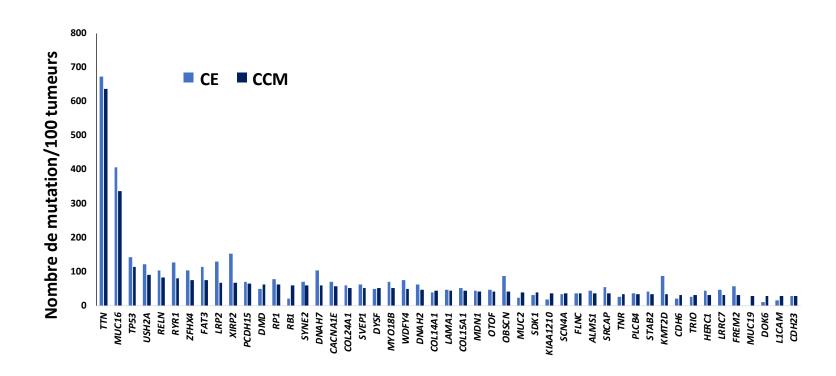
UV

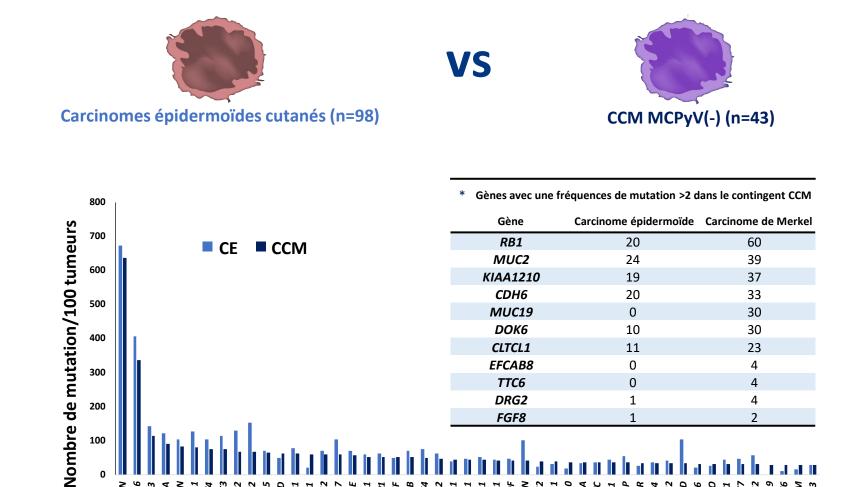
Évènement génétique spécifique



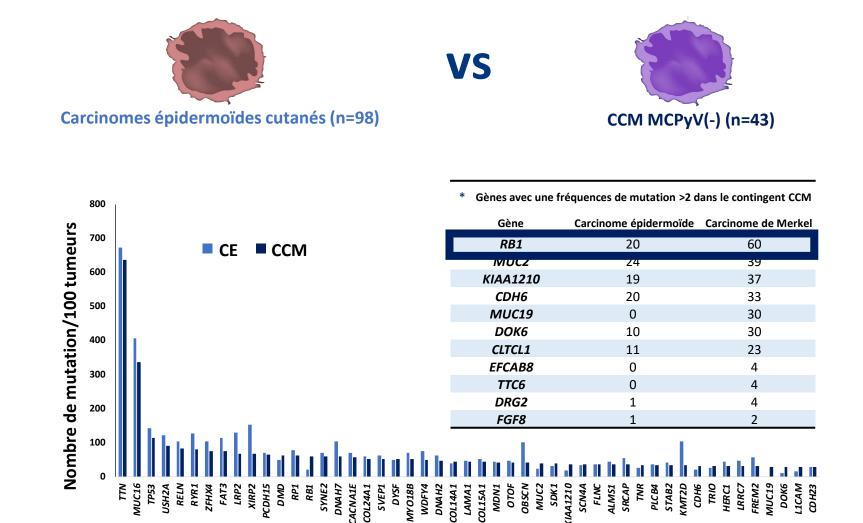








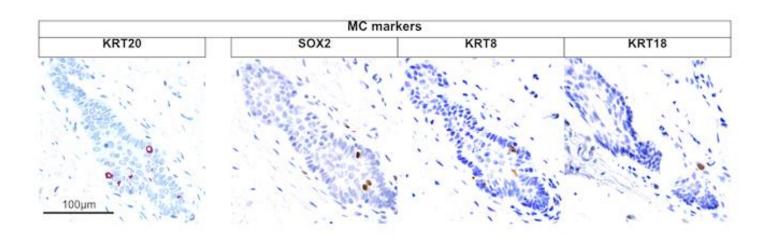
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MUC16
TP53
USH2A
RELN
RYR11
ZFHX4
FAT3
LRP2
XIRP2
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XIRP2
DNMD
RP1
RP1
SYNE2
DNAH7
COL24A1
SYNE2
DNAH7
OTOF
OBSCN
MUC2
SDK1
(IAAA1210
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FLNC
ALMS1
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HRC1
LRRC7
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DOK6
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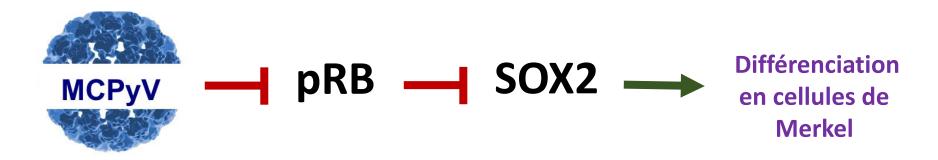
L'inactivation de RB1 induit le phénotype "Merkel"

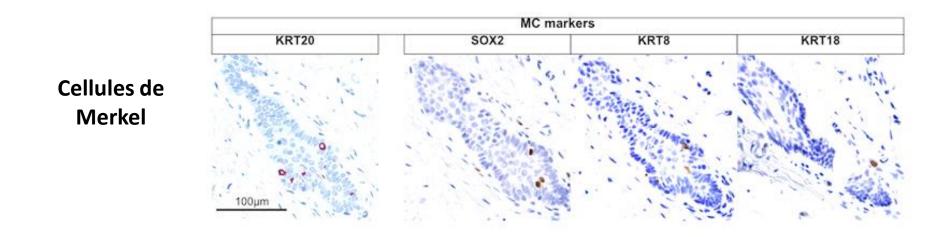


Cellules de Merkel



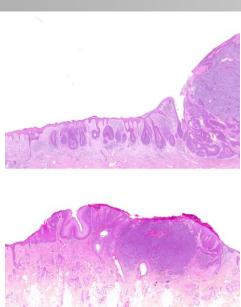
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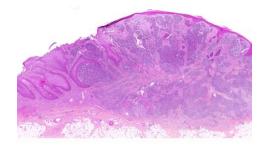




⇒ Les mutations inactivatrices de RB1 induisent la différenciation neuroendocrine au sein des Carcinomes épidermoïdes ?

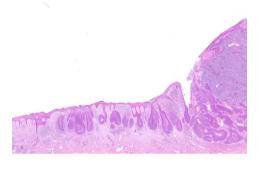
Mutation et expression de RB1 dans les CCM composites

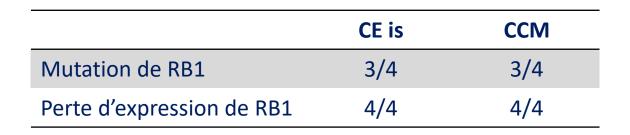


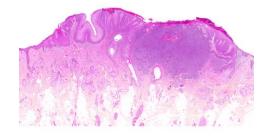


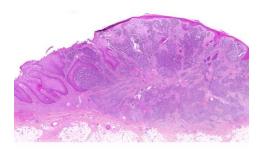


Mutation et expression de RB1 dans les CCM composites

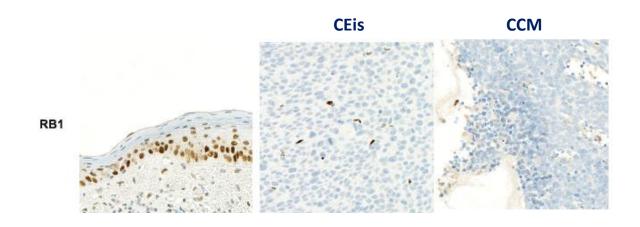






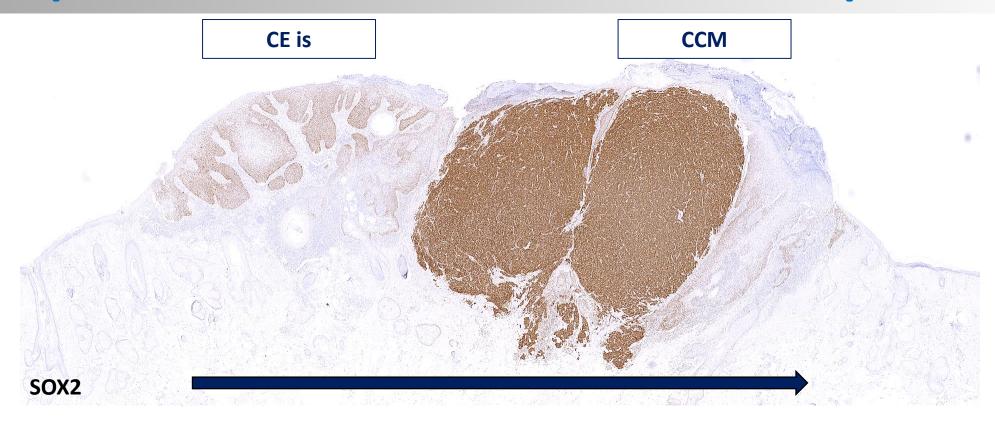




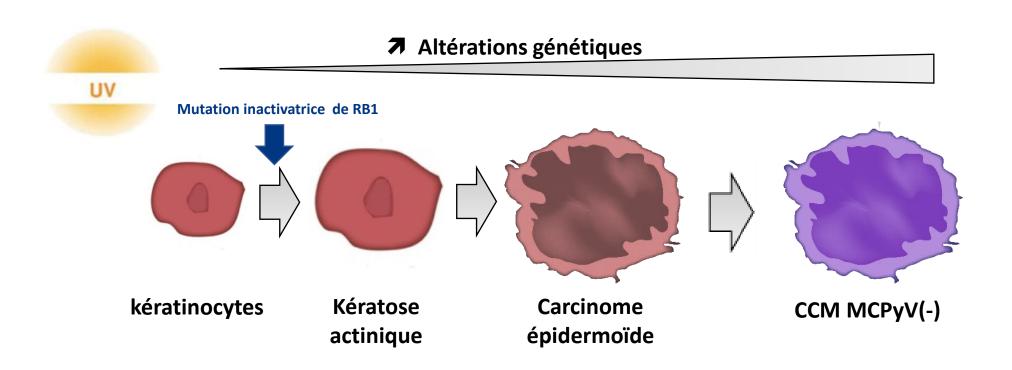


⇒ L'inactivation de RB1 est un évènement précoce au cours du développement des CCM

Expression de SOX2 dans les CCM composites

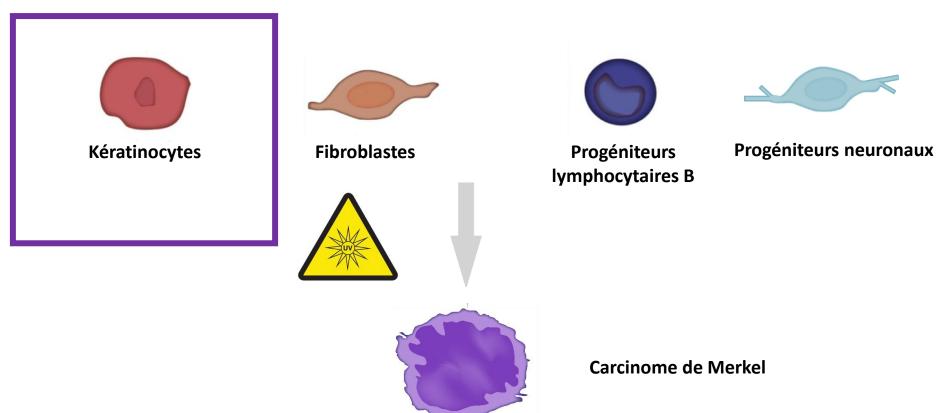






Conclusion

• Preuve de l'origine kératinocytaire des CCM-MCPyV(-)



Conclusion

• Preuve de l'origine kératinocytaire des CCM-MCPyV(-)

• Inactivation de RB1 : un prérequis au développement des CCM MCPyV(-)







Remerciements



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Plateforme de biologie moléculaire de Tours

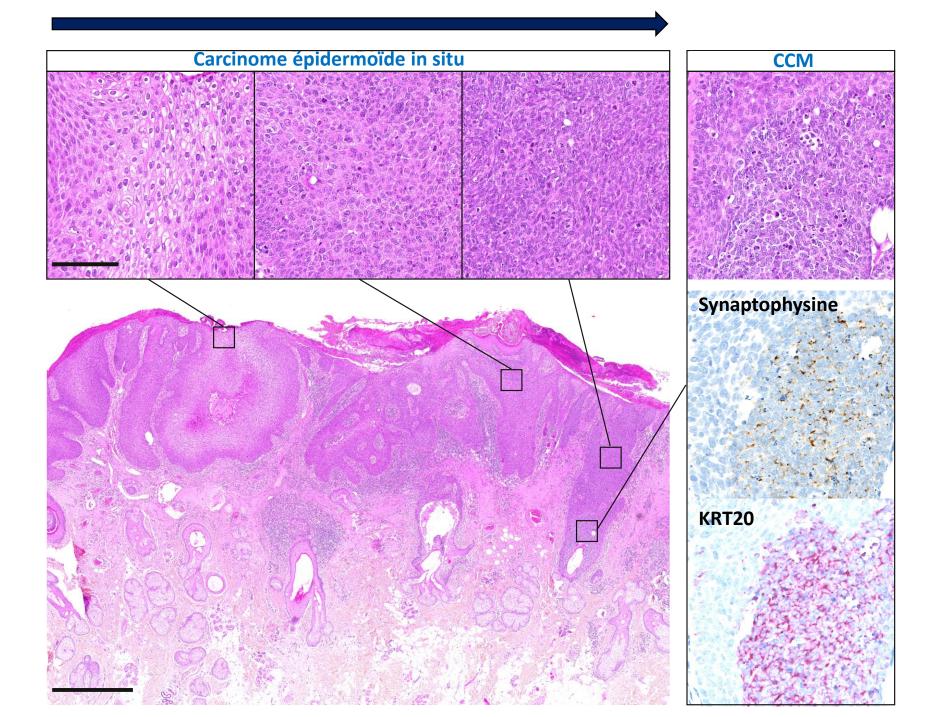
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Eric Frouin, Agnès Beby-Defaux



Analyse de l'exome

