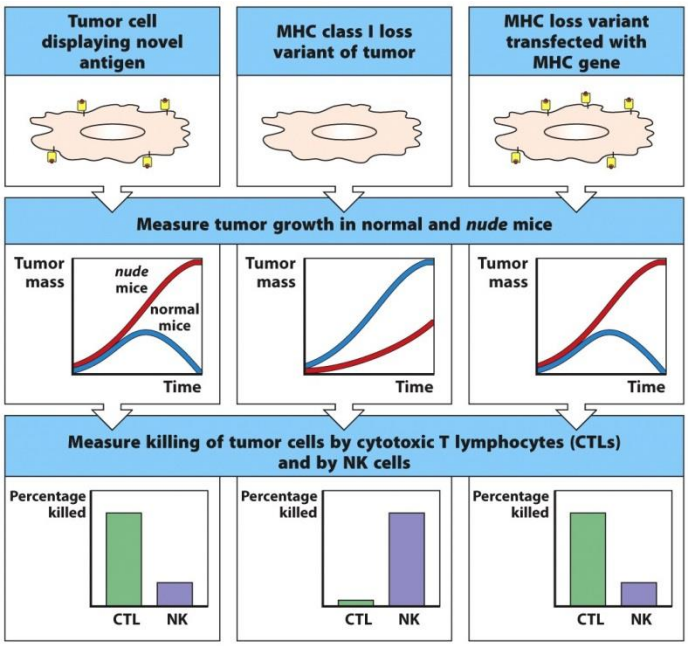
The effect of cytotoxic T cells and NK cells



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- Regression transplanted tumours due to CTLs
- Tumour variant with low MHCI, less sensitive to CTLs but more sensitive to NK cells
- *nude* mice = no T cells, more NK cells than normal
- Tumour rejection antigens = peptides of tumour cell proteins presented on MHC
- Target of tumour-specific response even though present on normal tissues e.g. strategy to induce response to melanoma antigen ➔ vitiligo

1) Normal mice will mount an immune response using mostly CTL, while nude mice will not be so successful at dealing with the tumour.

2) Tumour which is not displaying MHCI normal mice will not be successful at dealing with the tumour but nude mice which have increased numbers of NK cell dealt with the tumour faster and better.

3) Tumour lost MHCI, is supplied with an MHCI gene we are back to original scenario.

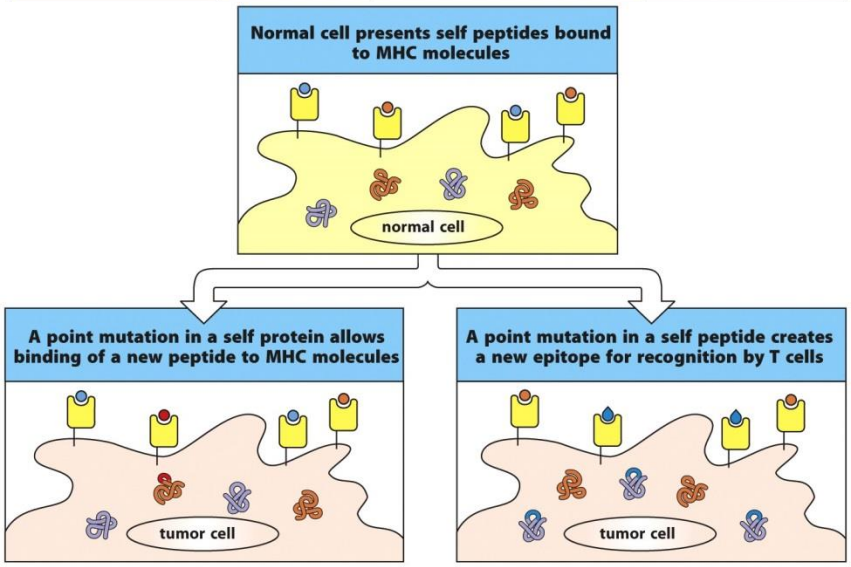
Potential tumor rejection antigens have a variety of origins

Class of antigen	Antigen	Nature of antigen	Tumor type
Tumor-specific mutated oncogene or tumor suppressor	Cyclin-dependent kinase 4	Cell-cycle regulator	Melanoma
	β-Catenin	Relay in signal transduction pathway	Melanoma
	Caspase 8	Regulator of apoptosis	Squamous cell carcinoma
	Surface Ig/ Idiotype	Specific antibody after gene rearrangements in B-cell clone	Lymphoma
Cancer-testis antigens	MAGE-1 MAGE-3 NY-ESO-1	Normal testicular proteins	Melanoma Breast Glioma
Differentiation	Tyrosinase	Enzyme in pathway of melanin synthesis	Melanoma

The reason certain types of proteins which are more liable to be tumour rejection antigens. It is often random and some of these proteins are not even cell surface antigens.

Tumour rejection antigens

- Point mutations or gene rearrangements occuring during oncogenesis.
- Proteins normally only expressed in male germ cells, male germ cells do not express MHC therefore these peptides not normally presented to T cells.
- Differentiation antigens, usually very tissue-specific, e.g. tyrosinase – normally only found in melanocytes.
- Tumour immunotherapy tries to harness and augment these responses.



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Potential tumor rejection antigens have a variety of origins

Class of antigen	Antigen	Nature of antigen	Tumor type
Abnormal gene expression	HER-2/neu	Receptor tyrosine kinase	Breast Ovary
	Wilms' tumor	Transcription factor	Leukemia
Abnormal post-translational modification	MUC-1	Underglycosylated mucin	Breast Pancreas
Abnormal post-transcriptional modification	GP100 TRP2	Retention of introns in the mRNA	Melanoma
Oncoviral protein	HPV type 16, E6 and E7 proteins	Viral transforming gene products	Cervical carcinoma

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