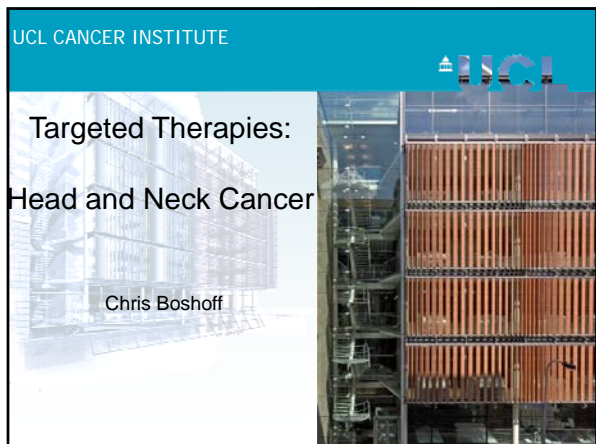
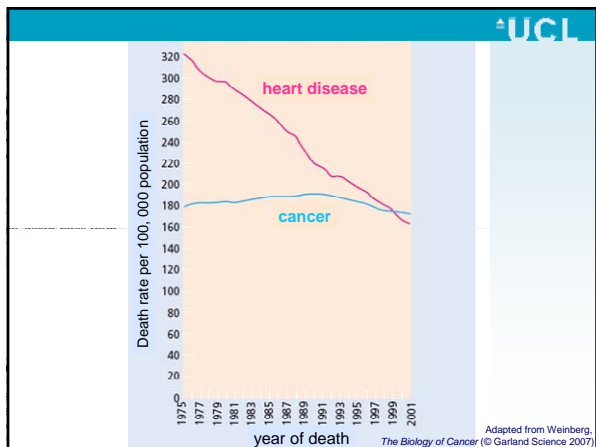


UCL CANCER INSTITUTE

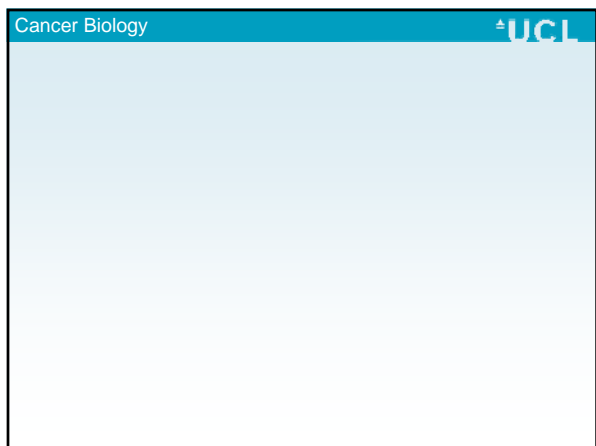
Targeted Therapies:
Head and Neck Cancer

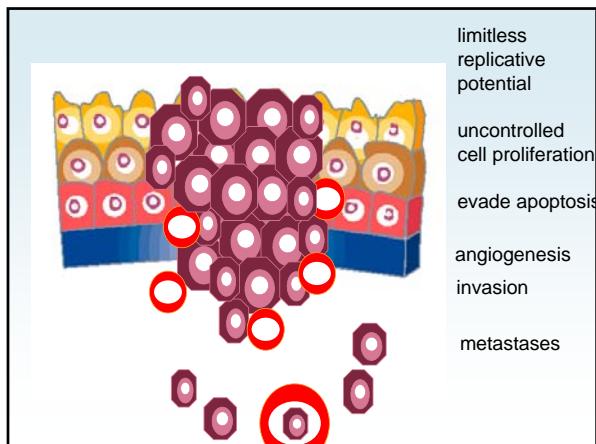
Chris Boshoff

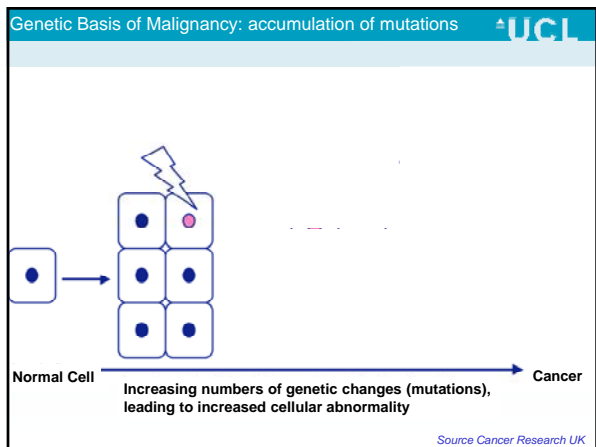


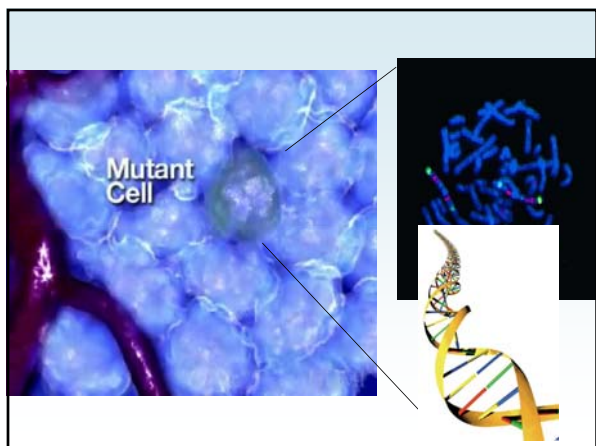


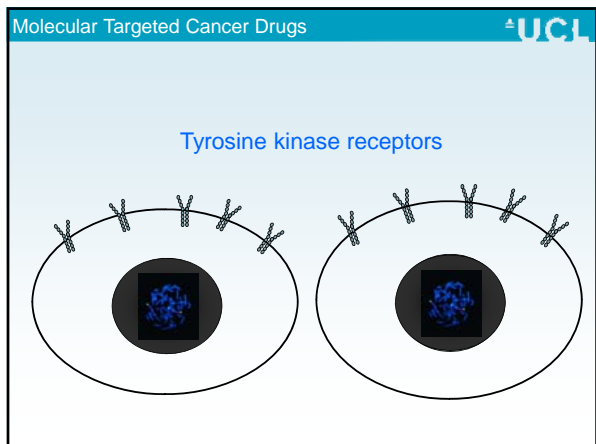
Cancer Biology

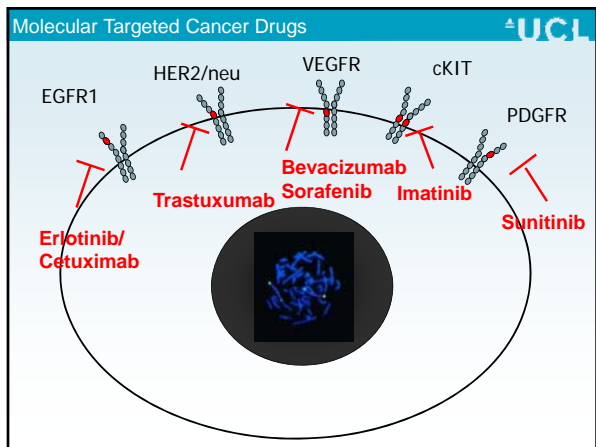






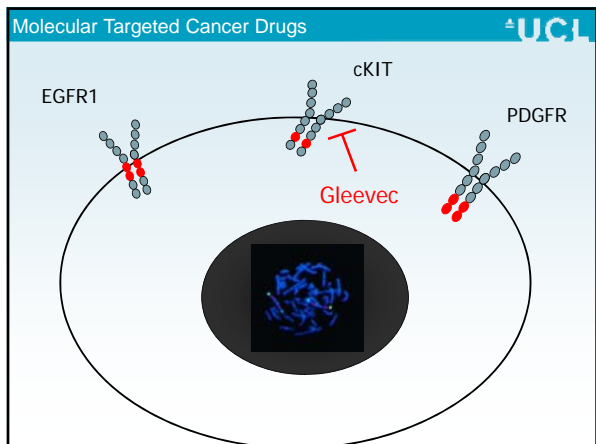


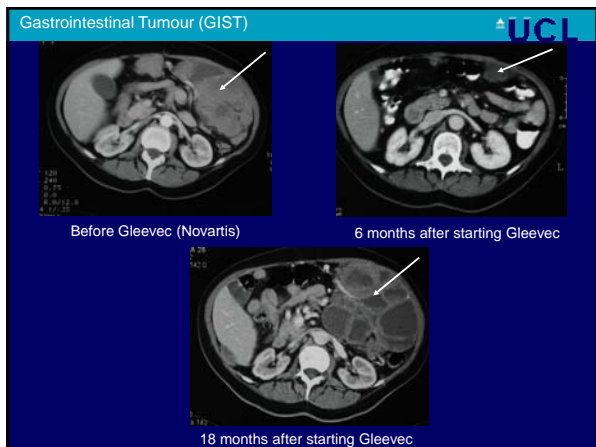


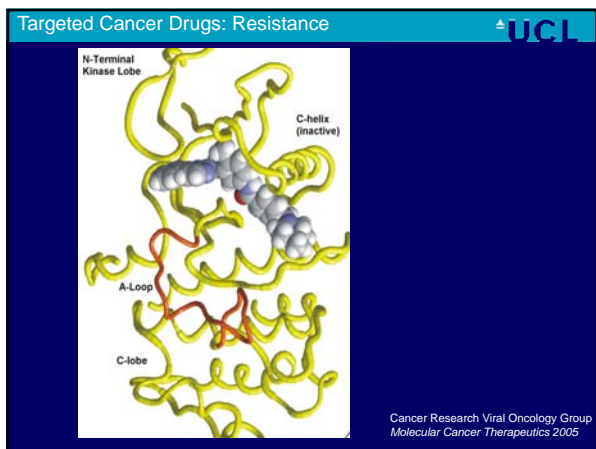


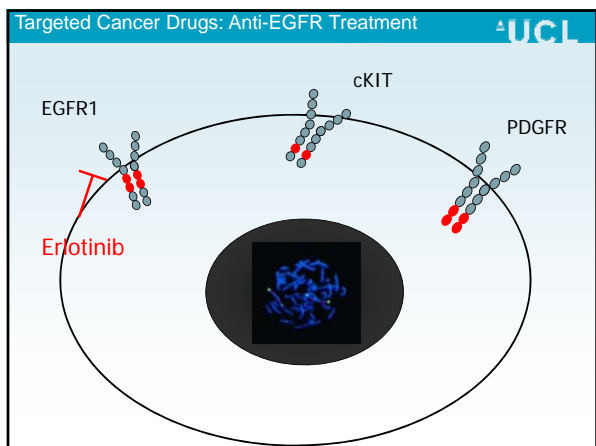
Tailored Treatment in Oncology UCL

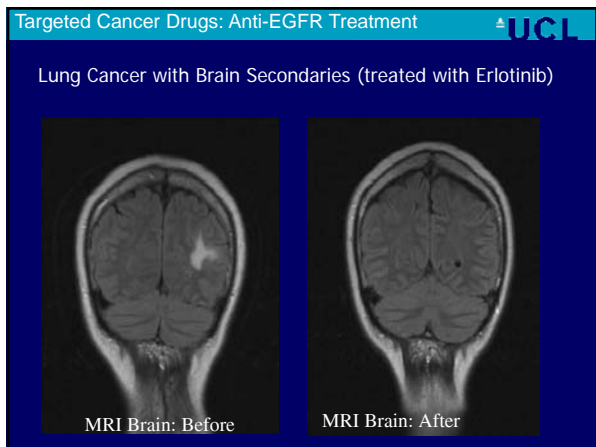
Tumor type	Drug	Biomarker predicting response
Gastrointestinal stromal tumor (GIST)	Imatinib Sunitinib	cKIT
Breast cancer	Trastuzumab	HER2
Metastatic colorectal cancer (mCRC)	Cetuximab	KRAS

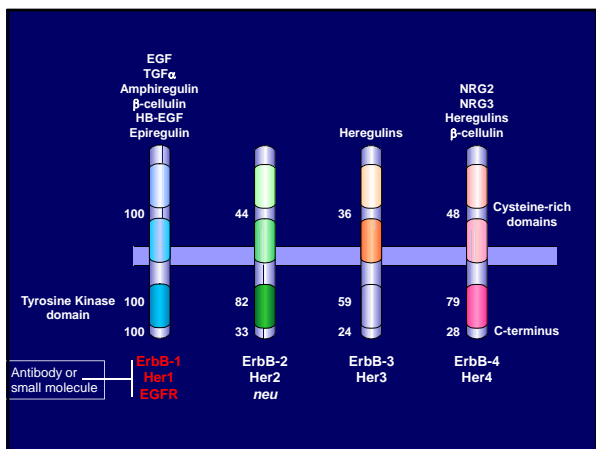


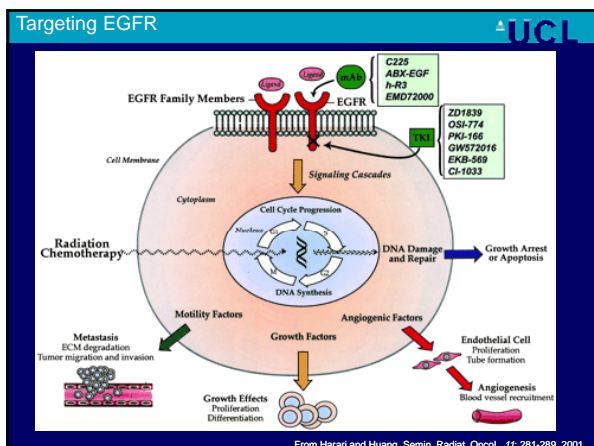


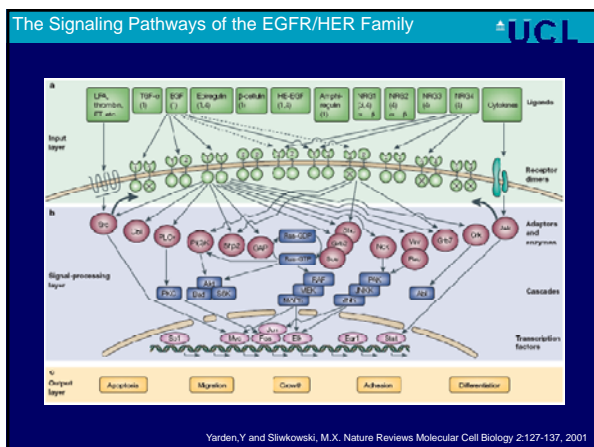












Targeting EGFR: Antibodies

Agent	Characteristic	Target	Tumor Type	Stage
Cetuximab	Chimeric	HER-1	Colon H&N, NSCLC, pancreas	Marketed Phase III
ABX-EGF	Human	HER-1	Colon, renal	Phase III
EMD-7200	Humanized	HER-1	H&N, ovarian, colon, cervix	Phase II
h-R3	Humanized	HER-1	H&N	Phase II
Pertuzumab	Humanized	HER-2	Breast, ovarian, prostate, NSCLC	Phase II
Trastuzumab	Humanized	HER-2	Breast	Marketed

Abbreviations: H&N, head and neck; NSCLC, non-small-cell lung cancer.

Baselga, J. and Arteaga, C.L. J Clin Onc 23: 2445-2459, 2005

Targeting EGFR: Small Molecules UCL

Table 2. Tyrosine Kinase Inhibitors Designed to Target the HER Family


Agent	Irreversible	Target	Tumor Type	Stage
Gefitinib	No	HER-1	NSCLC	Marketed
Erlotinib	No	HER-1	NSCLC, pancreas	Marketed
Lapatinib	No	HER-1/2	Breast	Phase III
CI-1033	Yes	Pan HER	SCC, skin	Phase II
EKB-569	Yes	HER-1	Colon	Phase II
BMS-599626	No	HER-1/2	—	Phase I
AEE788	No	HER-1/2 Anti-VEGFR	—	Phase I

Abbreviations: NSCLC, non-small-cell lung cancer; SCC, squamous cell carcinoma; VEGFR, vascular endothelial growth factor receptor.

Baselga, J. and Arteaga, C.L. J Clin Onc 23: 2445-2459, 2005

Targeting EGFR: Cetuximab UCL

C225, Cetuximab



- Chimerized antibody of the IgG1 subclass
- Highly specific for EGFR (ERB1)
 - Prevents ligand binding to EGFR
 - Stimulates receptor internalization
 - Blocks receptor dimerization, TK activity, phosphorylation, and signal transduction
- Cetuximab alone, or with combination with cytotoxics has activity in colorectal, lung, and head & neck cancer
 - FDA-approval for refractory colorectal cancer in 2004 and locally advanced/metastatic head & neck cancer 2006

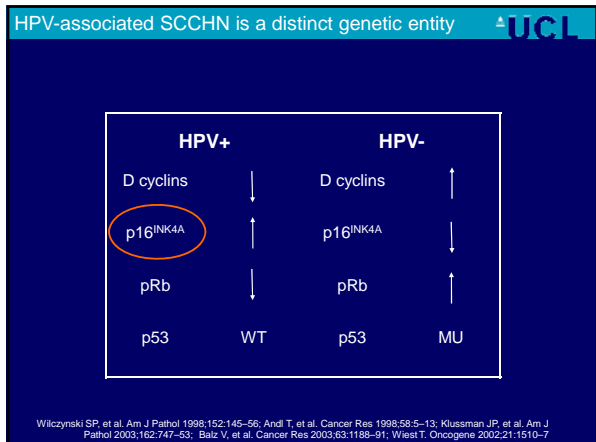
Cetuximab in Head & Neck Cancer UCL

Clinical Efficacy in Locoregionally Advanced SCCHN

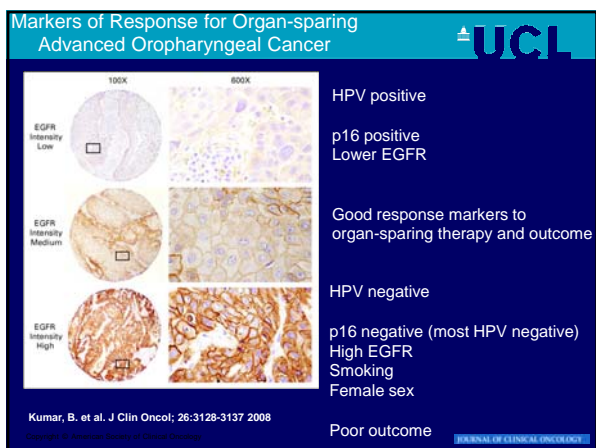
	Cetuximab + Radiation (n=211)	Radiation Alone (n=213)	Hazard Ratio (95% CI)*	Stratified Log-rank p-value
Locoregional control Median duration	24.4 mo	14.9 mo	0.68 (0.52-0.89)	0.005
Overall survival Median duration	49.0 mo	29.3 mo	0.74 (0.57-0.97)	0.03

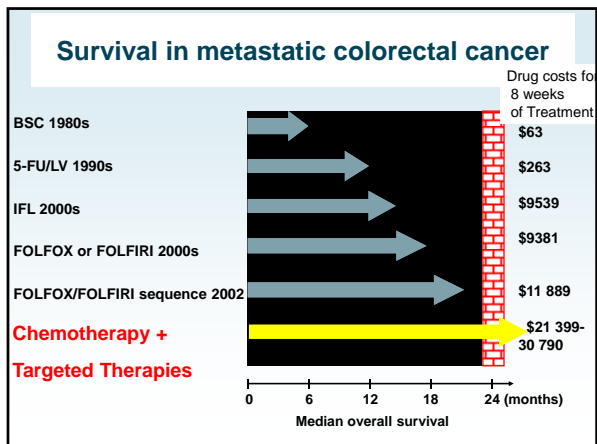
* CI = confidence interval.

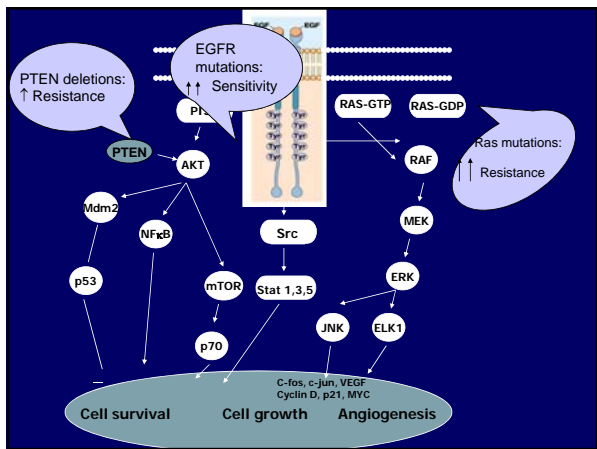
Bonner, NEJM

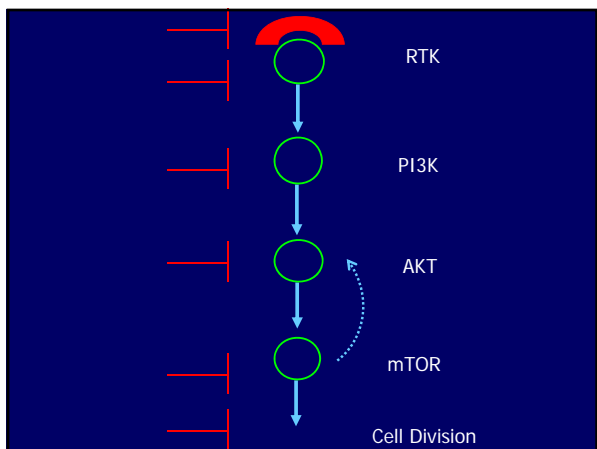













Tailored therapy for SCCHN? 

- Future investigations will elucidate biomarkers to predict the efficacy of targeted therapies in individual patients
- No clinically relevant biomarker for Cetuximab in SCCHN to date
- Understanding Genetic Basis will lead to more Rational Design of Combination Therapies

In future, a systems medicine-based approach could be employed for tailored therapy

