“INTERDISCIPLINARY TUMOR CENTER (ITC) MAINZ”

AT THE JOHANNES GUTENBERG-UNIVERSITY IN MAINZ

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3 Cancer Center Director and Deputy Directors

The Cancer Center is directed by an Executive Board composed of representatives of the three clinical key disciplines Medical Oncology, Radiation Oncology and Surgical Oncology.

3.1 Cancer Center Director

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Biographical sketch with research focus:

Thomas Wölfel (*1956) has been senior physician since 1997 and Associate Professor in Hematology / Oncology since 1999 at the Johannes Gutenberg-University of Mainz (III. Department of Internal Medicine, chaired by Professor Christoph Huber). He finished his medical thesis in 1983 and performed his post-doctoral work from 1984 to 1987 in the laboratory of Professor Thierry Boon at the Ludwig Institute for Cancer Research in Brussels.

He is a broadly educated oncologist certified by the ESMO in 1998. Since 2003 he is a driving force of the interdisciplinary tumor center (ITC) Mainz. He served as its executive director in its developmental phase, founded and moderates interdisciplinary oncology board meetings and is dedicated to the development of graduate education and training programs and to continuing education both in preclinical and clinical science. Since 2003 he is a board member of the national CME (continued medical education) initiative MTTC (Molecular Targeted Therapy of Cancer).

T. Wölfel is an internationally renowned tumor immunologist who pioneered the discovery of individual tumor antigens recognized by T lymphocytes (Ref. 2). Since 1988, he has benefited from continuous grant support by the German Research Council, the German Cancer Aid and the European Community. Since 1997, he has been principal investigator, co-investigator and laboratory investigator in cancer immunotherapy trials. His research group focuses on the identification of preferential targets for the individual anti-tumor T cell repertoire (Ref. 10) and their impact on cancer immunotherapy.

Memberships:

- European Society for Medical Oncology (ESMO) (certified member),
- German Society for Hematology and Oncology (DGHO),
- German Cancer Society (DKG),
- Society of Medical Oncology (AIO) within the German Cancer Society,
- German Society for Internal Medicine (DGI),
- Association for Immunotherapy of Cancer (www.c-imt.org; founder member, program director).

Selected publications:

1. De Plaen, E., C. Lurquin, A. Van Pel, B. Mariame, J.-P. Szikora, T. Wölfel, C. Sibille, P. Chomez, and T. Boon. 1988. Immunogenic (tum$^-$) variants of mouse tumor P815: Cloning of the gene of tum$^-$ antigen P91A and identification of the tum$^-$ mutation. Proc. Natl. Acad. Sci. USA 85: 2274-2278.
2. Wölfel, T., E. Klehmann, C. Müller, K.-H. Schütt, K.-H. Meyer zum Büschenfelde, and A. Knuth. 1989. Lysis of human melanoma cells by autologous cytolytic T cell (CTL) clones: Identification of HLA-A2 as a restriction element for three different antigens. J. Exp. Med. 170: 797-810.
3. Brichard V., A. Van Pel, T. Wölfel, C. Wölfel, E. de Plaen, B. Lethé, P. Coulie, and T. Boon. 1993. The tyrosinase gene codes for an antigen recognized by autologous cytolytic T lymphocytes on HLA-A2 melanomas. J. Exp. Med. 178: 489-495.
4. Wölfel, T., A. Van Pel, V. Brichard, J. Schneider, B. Seliger, K.-H. Meyer zum Büschenfelde, and T. Boon. 1994. Two tyrosinase nonapeptides recognized on HLA-A2 melanomas by autologous cytolytic T lymphocytes. Eur. J. Immunol. 24: 759-764.
5. Wölfel T., M. Hauer, J. Schneider, M. Serrano, C. Wölfel, E. Klehmann-Hieb, E. De Plaen, T.Hankeln, K.-H. Meyer zum Büschenfelde, and D. Beach. 1995. A p16^{INK4a}-insensitive CDK4 mutant targeted by cytolytic T lymphocytes in a human melanoma. Science 269: 1281-1284.
6. Skipper J. C. A., R. C. Hendrickson, P. H. Gulden, V. Brichard, A. Van Pel, Y. Chen, J. Shabanowitz, T. Wölfel, G. L. Slingluff Jr., T. Boon, D. F. Hunt, and V. H. Engelhard. 1996. An HLA-A2-restricted tyrosinase antigen on melanoma cells resulted from posttranslational modification and suggests a novel pathway for processing of membrane proteins. J. Exp. Med. 183: 527-534.
7. Herr W., B. Linn, N. Leister, E. Wandel, K.-H. Meyer zum Büschenfelde, and T. Wölfel. 1997. The use of computer-assisted video image analysis for the quantification of CD8$^+$ T lymphocytes producing tumor necrosis factor a spots in response to peptide antigens. J. Immunol. Methods 203: 141-152.
8. Drexler I., E. Antunes, M. Schmitz, T. Wölfel, C. Huber, V. Erfle, E. P. Rieber, M. Theobald, and G. Sutter. 1999. Modified vaccinia virus Ankara for delivery of human tyrosinase as melanoma-associated antigen: induction of tyrosinase- and melanoma-specific HLA-A*0201-restricted cytotoxic T cells *in vitro* and *in vivo*. Cancer Res. 59: 4955-4963.
9. Konopitzky R., U. König, R. G. Meyer, W. Sommergruber, T. Wölfel, and T. Schweighoffer. 2002. Identification of HLA-A*0201-restricted T cell epitopes derived from the novel overexpressed tumor antigen CLCA2. J. Immunol. 169: 540-547.
10. Lennerz V., M. Fatho, C. Gentilini, R. A. Frye, A. Lifke, D. Ferel, C. Wölfel, C. Huber, and T. Wölfel. 2005. The response of autologous T cells to a human melanoma is dominated by mutated neoantigens. Proc. Natl. Acad. Sci. USA 102: 16013-16018.

3.2 1st Deputy Director

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Biographical sketch with research focus:

Heinz Schmidberger (*1960) is Professor of Radiation Oncology and the Head of the Department of Radiation Oncology at the University Hospital of Mainz.

He received his medical education at the University of Ulm, the University of Tübingen (Germany), and the University of Liverpool (GB). He graduated from medical school in Tübingen in 1987 and received a scholarship of the Rotary Foundation to pursue a postdoctoral fellowship in radiobiology and tumor immunology at the University of Minnesota in Minneapolis (USA). From 1989 to 1994 Dr. Schmidberger received his clinical training in Radiation Oncology at the University of Tübingen. From 1995 to 2005 Dr. Schmidberger has been working as a senior Radiation Oncologist at the University of Göttingen. After 2000 he was also a senior lecturer at the faculty.

On April 2005, Dr. Schmidberger has been appointed Professor of Radiation Oncology and Head of the Department of Radiation Oncology at the University of Mainz.

Research Focus:

- radiotherapy in Testicular Cancer,
- radiotherapy in Malignant Lymphoma,
- multimodal therapy in gastrointestinal cancer,
- modification of intrinsic radio sensitivity of tumor cells,
- cellular communication and late effects of radiation in normal tissues.

Memberships:

- German Testicular Cancer Study Group and the European Germ Cell Cancer Consensus Group,
- reference radiotherapist in all multicenter lymphoma study groups in Germany,
- Study coordinator of the ARO (Arbeitsgemeinschaft Radioonkologie) of the German Cancer society,
- ESTRO, ASTRO, DEGRO, German Cancer Society.

Selected publications:

1. Schmidberger, H., P. Virsik-Peuckert, M. Rave-Fränk, K.-R. Reinosch, O. Pradier, and C.F. Hess. 2001. Reciprocal translocations in patients with testicular seminoma before and after radiotherapy. Int. J. Radiat. Oncol. Biol. Phys. 50: 857-864.
2. Pradier, O., M. Rave-Fränk, J. Lehmann, E. Lücke, O. Boghun, C.F. Hess, and H. Schmidberger. 2001. Effects of docetaxel in combination with radiation on human head and neck cells (ZMK-1), and cervical squamous cell carcinoma (CaSki). Int. J. Cancer 91: 840-5.
3. Rave-Frank, M., P. Virsik-Kopp, O. Pradier, M. Nitsche, S. Grunefeld, and H. Schmidberger. 2001. In Vitro Response of Human Dermal Fibroblasts to X-Irradiation: Relationship Between Radiation-Induced Clonogenic Cell Death, Chromosome Aberrations and Markers of Proliferative Senescence or Differentiation. Int. J. Radiat. Biol. 77: 1163-74.
4. Schmidberger, H., M. Rave-Fränk, J. Lehmann, E. Weiss, L. Gerl, N. Dettmar, S. Glomme, and C.F. Hess. 2003. Lack of interferon-beta-induced radiosensitization in four out of five human glioblastoma cell lines. Int. J. Radiat. Oncol. Biol. Phys. 55: 1348-1357.
5. Virsik-Köpp, P., M. Rave-Fränk, H. Hofman-Hüther, H. Schmidberger. 2003. The role of DNA-PK in the process of aberration formation as studied in irradiated human glioblastoma cell lines MO59K and MO59J. Int. J. Radiat. Biol. 73: 61-68.
6. Virsik-Köpp, P., M. Rave-Fränk, H. Hofman-Hüther, and H. Schmidberger. 2004. Role of DNA-dependent protein kinase in the process of radiation-induced aberration formation. Int. J. Radiat. Biol. 80:125-133.
7. Classen, J., H. Schmidberger, C.H. Meisner, C. Winkler, J. Dunst, R. Souchon, L. Weissbach, V. Budach, W. Alberti, M. Bamberg. 2004. Paraaortic irradiation for stage I testicular seminoma: Results of A prospective study in 675 patients. Br. J. Cancer 90: 2305-2311.
8. Sauer, R., H. Becker, W. Hohenberger, C. Rodel, C. Wittekind, R. Fietkau, P. Martus, J. Tschmelitsch, E. Hager, C.F. Hess, J.H. Karstens, T. Liersch, H. Schmidberger, R. Raab, and the German Rectal Cancer Study Group. 2004. Preoperative versus postoperative chemoradiotherapy for rectal cancer. *N Engl J Med* 351: 1731-1740.
9. Virsik-Kopp P., H. Hofman-Huther, M. Rave-Frank, and H. Schmidberger. 2005. The effect of wortmannin on radiation-induced chromosome aberration formation in the radioresistant tumor sell line WiDr. Radiat. Res. 164: 148-156.
10. Christiansen H., S. Koenig, P. Krause, R.M. Hermann, M. Rave-Frank, T. Proehl, H. Becker, C.F. Hess, and H. Schmidberger. 2006. External-beam radiotherapy as preparative regimen for hepatocyte transplantation after partial hepatectomy. Int. J. Radiat. Oncol. Biol. Phys. 65:509-516.

3.3 2nd Deputy Director

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Biographical sketch with research focus:

Joachim Thüroff received his urological training (1978 – 1981) at the Department of Urology, Johannes Gutenberg-University, Mainz (Chairman: Professor Dr. R. Hohenfellner). He was Associate Professor of Urology in Mainz (1981 – 1985) and San Francisco (University of California, San Francisco, 1985 – 1987).

Joachim Thüroff was Chairman of the Department of Urology, Klinikum Wuppertal (1987 – 1997) and Professor of Urology of the University of Witten-Herdecke. Since 1997 he is Professor and Chairman of the Department of Urology, Johannes Gutenberg-University, Medical School, Mainz.

Joachim Thüroff is member in numerous national and international scientific societies, of which the following have an uro-oncological focus:

- Society for Urological Oncology (AUO),
- European Intra-Renal Surgery Society (EIRSS),
- the Society of Pelvic Surgeons (SPS), and the
- American Association of Genitourinary Surgeons (AAGUS).

As President or Co-chairman he organized 27 national and international scientific meetings and was President of the Deutsche Gesellschaft für Urologie (DGU) in 2004 and organized its annual meeting.

In the urological laboratory and the clinical Department of Urology, uro-oncological research is focused on renal cell cancer, bladder cancer and prostate cancer, both in basic research and clinical trials. He is founding member of the Interdisciplinary Tumor Center (ITC) – Mainz. Surgical Fields of special uro-oncological expertise are radical perineal and retro pubic nerve sparing prostatectomy, open-surgical and laparoscopic radical nephrectomy and nephron-sparing tumor excision, and radical cystectomy with continent orthotopic or cutaneous bladder substitution (Mainz-Pouch I) or continent and urinary diversion (Mainz-Pouch II).

Selected publications:

1. Brenner, W., G. Färber, T. Herget, H.-A. Lehr, J.G. Hengstler, and J.W. Thüroff. 2002. Loss of the tumor suppressor protein PTEN during renal carcinogenesis. Int. J. Cancer 99: 53-57.
2. Filipas, D., C. Spix, D. Schulz-Lampel, J. Michaelis, R. Hohenfellner, S. Roth, and J.W. Thüroff. 2003. Screening for renal cell carcinoma using ultrasonography: a feasibility study. BJU Int. 9: 595-599.
3. Brenner, W., G. Färber, T. Herget, C. Wiesner, J.G. Hengstler, and J.W. Thüroff. 2003. Protein Kinase C eta is associated with progression of renal cell carcinoma (RCC): a systematic study of eleven PKC-isoforms in RCC in relation to histopathological parameters. Anticancer Res. 23: 4001-4006.
4. Brenner, W., C. Wiesner, G. Färber, T. Herget, J.G. Hengstler, and J.W. Thüroff. 2003. Gender specific expression of tumor suppressor PKCδ versus oncogenic PKCη in renal cell carcinoma. EXCLI J. 2: 45-51.
5. Reinhard, H., O. Semler, D. Burger, U. Bode, M. Flentje, U. Gobel, P. Gutjahr, I. Leuschner, E. Maass, F. Niggli, H.G. Scheel-Walter, M. Stöckle, J.W. Thüroff, J. Troger, A. Weirich, D. von Schweinitz, A. Zoubek, and N. Graf. 2004. Results of the SIOP 93-01/GPOH trial and study for the treatment of patients with unilateral nonmetastatic Wilms Tumor. Klin. Padiatr. 216: 132-140.
6. Leissner, J., M.A. Ghoneim, H. Abol-Enein, J.W. Thüroff, L. Franzaring, M. Fisch, H. Schulze, G. Managadze, P. Allhoff, M.A. El-Baz, H. Kastendieck, P. Buhtz, S. Kropf, R. Hohenfellner, and H.K. Wolf. 2004. Extended radical lymphadenectomy in patients with urothelial bladder cancer: Results of a prospective multicenter study. J. Urol. 171: 139-144.
7. GillITCer, R., S.W. Melchior, C. Hampel, C. Wiesner, J. Fichtner, and J.W. Thüroff. 2004. Specific complications of radical perineal prostatectomy: a single institution study of more than 600 cases. J. Urol. 172: 124-128.
8. Filipas, D., M. Fisch, R. Stein, P. Gutjahr, R. Hohenfellner, and J.W. Thüroff. 2004. Rhabdomyosarcoma of the bladder, prostate or vagina: the role of surgery. BJU Int. 93: 125-129.
9. Brenner, W., F. Benzing, J. Gudejko-Thiel, R. Fischer, G. Färber, J.G. Hengstler, B. Seliger, and J.W. Thüroff. 2004. Regulation of b1 integrin expression by PKCepsilon in renal cancer cells. Int. J. Oncol. 25: 1157-1163.
10. Wiesner, C., J. PflTCenmaier, A. Faldum, R. GillITCer, S.W. Melchior, and J.W. Thüroff. 2005. Lymph node metastases in non-muscle invasive bladder cancer are correlated with the number of transurethral resections and tumour upstaging at radical cystectomy. BJU Int. 95: 301-305.
11. Lehmann, J., M. Retz, C. Wiemers.,J. Beck., J. Thüroff, C. Weining, P. Albers, D. Frohneberg, T. Becker, P.J. Funke, P. Walz, S. Langbein, F. Reiher, M. Schiller, K. Miller, S. Roth, T. Kalble, D. Sternberg, S. Wellek, and M. Stöckle. 2005. Adjuvant cisplatin plus methotrexate versus methotrexate, vinblastine, epirubicin, and cisplatin in locally advanced bladder cancer: results of a randomized, multicenter, phase III trial (AUO-AB 05/95). J. Clin. Oncol. 23: 4963-74.

4 Plan of the hospital / university campus

The Hospital of the Johannes Gutenberg-University was built in 1914. It was continuously modernized during the past decades. One major investment of the recent years is a central building (building 605) for all departments of internal medicine including clinical chemistry as well as diagnostic imaging and imaging–guided interventions that will be functional in fall 2006 (see http://www.klinik.uni-mainz.de/). As a consequence the building 403 (**Figures 1** and **2**) will be available to accommodate the ITC core activities. This will include a centralized outpatient clinic for new admissions and consultations as well as systemic chemotherapy and supportive therapy. These facilities will be shared by the ITC partners.

Figure 1: Plan of the Hospital

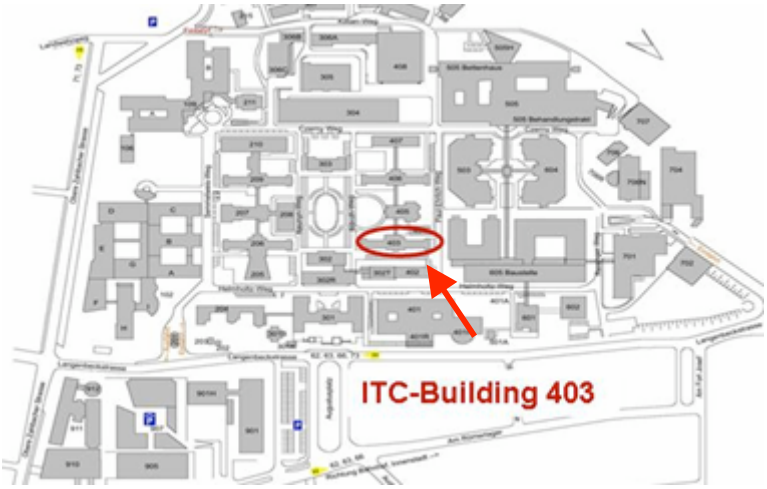

Figure 2: ITC Building 403

5 Support

The President of the Johannes Gutenberg-University, the Dean of the Medical Faculty together with the directors of institutes and departments of the University Hospital (http://www.klinik.uni-mainz.de/), that are involved in oncological research and patient care, strongly support the ITC development and its acitivities.

6 Organizational structure and responsibilities of the Cancer Center

In Germany the oncology service is in transition from departmental structures to interdisciplinary disease-oriented patient care. This development is clearly boosted by new systemic treatment options that evolved at rapid pace during the recent years. The development of new multimodal treatment strategies involving systemic therapy, radiotherapy and surgery is mandatory. These challenges can be met best within comprehensive cancer centers (CCC), that

- offer cost-effective centralized process structures and thereby facilitate quality control,
- enable fast and reliable synchronization of interdisciplinary efforts,
- accelerate the translation of basic research and the integration of innovative findings from other areas, and
- facilitate integrative education and postdoctoral training.

The Mainz University Hospital set out to stepwise prepare the formation of a CCC equivalent. In late 2003 the Hospital formally initiated the development of an Interdisciplinary Tumor Center (**ITC Mainz**). The **organizational structure** of the ITC is illustrated in **Figure 3**. The members of the *ITC Executive Board* are appointed every five years by the *Executive Board of the Hospital* („Klinikvorstand“). The *ITC Executive Board* consists of a Cancer Center Director (T. Wölfel/Medical Oncology) with full-time commitment towards the ITC, and two Deputy Directors (H. Schmidberger/Radiation Oncology and J.W. Thüroff/Surgical Oncology) with part-time commitment. They are supported by the *ITC Advisory Board*. Advisers are representatives of various clinical and theoretical disciplines with a strong focus on oncology that are renowned experts in their respective fields. In addition, external advisers will be appointed. Integral parts of the ITC are the Interdisciplinary Outpatient Clinic and interdisciplinary Disease Management Groups (DMGs) to be organized and supported by ITC personnel.

With respect to **responsibilities and goals** of the ITC, the *ITC Executive Board* defines the strategic focuses of the ITC and, together with the ITC personnel, further develops the core activities of the ITC. These activities are as follows:

- to organize DMG boards, meetings and protocol recording (Chapter 10.3, p 21);
- an interdisciplinary outpatient clinic for new admissions and consultations as well as centralized systemic chemotherapy and supportive therapy cooperatively directed by T. Wölfel (Medical Oncology), S. Kanzler (Gastrointestinal Oncology) and M. Schmidt (Gyneco-Oncology);
- to promote the development of quality assessment;
- the establishment of a comprehensive clinical cancer registry (Chapter 12, p 30);
- to promote, support and organize interactive and interdisciplinary preclinical and clinical research;
- to promote teaching of undergraduates and health professionals, and
- to provide continuing medical education as well as outreach programs.

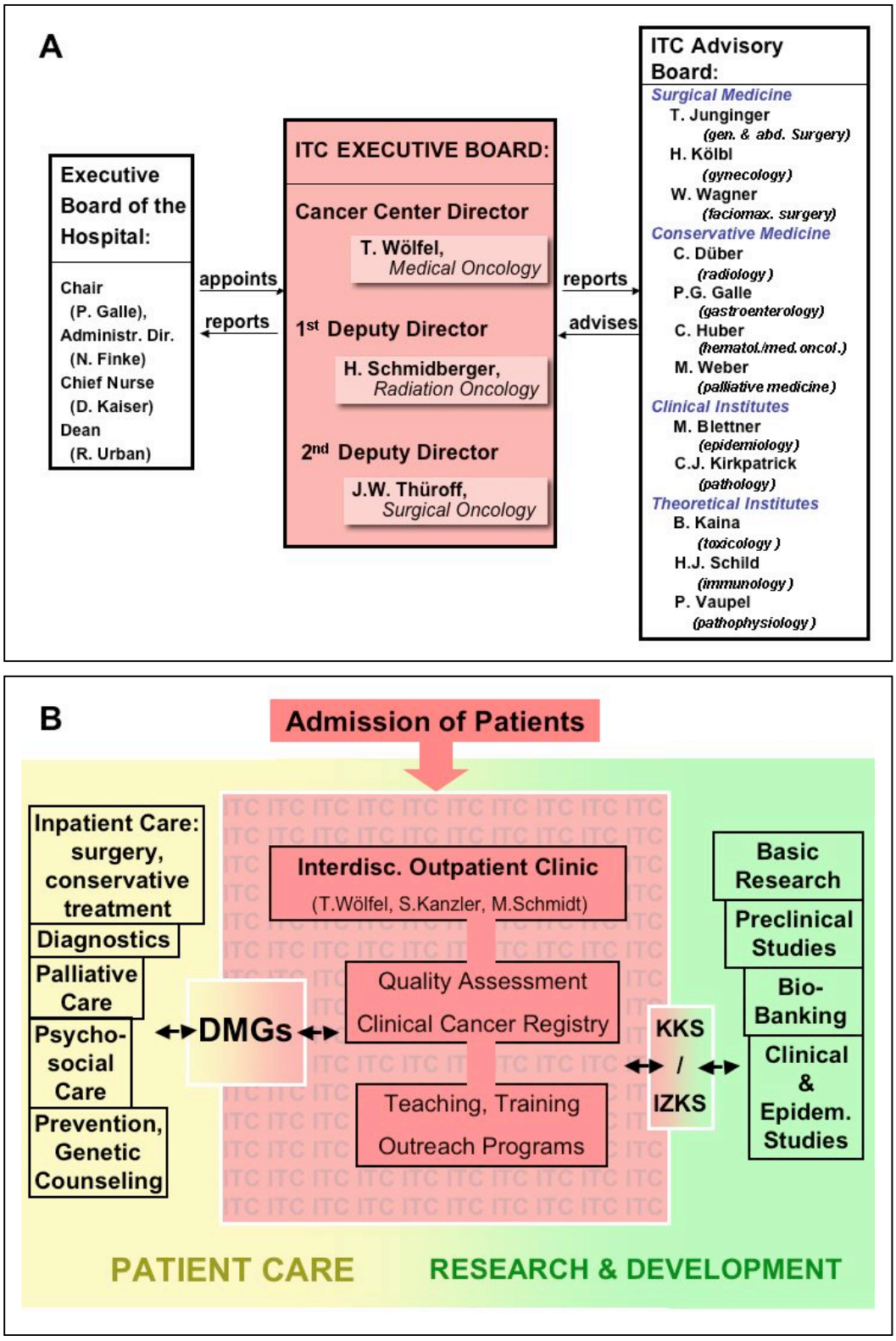

Figure 3: Organizational structure, responsibilities (**A**) and activities of the ITC (**B**).

Abbreviations: DMG=Disease Management Group, KKS= Coordinating Center of Clinical Studies, IZKS=Interdisciplinary Center for Clinical Studies (in the planning phase)

7 Summary of current laboratory and clinical research activities

The Members of the Medical Faculty are clearly determined to develop research-driven approaches for the improvement of cancer treatment and control.

Activities in basic and preclinical research cover a wide range of topics relevant to oncology. Examples of focused research activities with long-term commitment are

- the study of cancer susceptibility, carcinogenesis and oncogenic signaling as well as mechanisms of resistance to therapeutic interventions (F. Oesch, B. Kaina/Institute of Toxicology; S. & D. Strand, P. Galle/I. Dept. of Internal Medicine; B. Zabel/Dept. of Pediatrics; M. Schuler and T. Fischer/III. Dept. of Internal Medicine);
- the study of the impact of micro environmental factors on malignant behavior and therapeutic intervention (e.g. radiotherapy) (P. Vaupel, W. Müller-Klieser and colleagues/Inst. of Physiology and Pathophysiology), and
- the Faculty Members' contributions to tumor immunology and cancer immunotherapy: They emanated from a decade-long investment in clinical immunology. Several clinical departments and institutions formed three distinct combined research groups chaired by C. Huber (Hematology/Oncology), J. Knop (Dermatology) and S. Bhakdi (Inst. of Medical Microbiology and Hygiene) and contribute to national and international tumor immunology programs. Pioneering basic and translational research projects led to early interventional trials and to the foundation of spin-off companies. In recognition of this, the State Government of Rhineland-Palatinate decided to fund the Immunology Cluster of Excellence "Immunointervention" (http://www.ice-mainz.de/).

Clinical Research is performed by established clinical research units, devoted to conducting disease-specific clinical trials. Current trials address the complete spectrum of innovative approaches such as therapeutic vaccination, antibody therapy, hematopoetic stem cell transplantation, anti-angiogenesis and signal transduction inhibition (Chapter 10.7, p 24). The hospital of the Johannes Gutenberg-University Mainz was among the first university hospitals in Germany to establish a Coordinating Center of Clinical Studies (KKS) (Chapter 10.7 A, p 24). It strengthens the scientific infrastructure for planning, performance, and assessment of clinical studies in accordance with international scientific standards. The Faculty's Institute for Medical Biometry, Epidemiology and Informatics (IMBEI) conducts the epidemiologic cancer registry of Rhineland-Palatinate and the renowned German Childhood Cancer Registry (GCCR). It has a high international reputation in cancer epidemiology research as well as in statistical methods for clinical trials.

Integrated graduate and postgraduate training programs set up during the recent years intensify and improve the promotion of young scientists in oncology.

Infrastructure and specialized technical Know-How are guaranteed by core facilities and technology providers such as

- an Animal Facility (directed by K. Reifenberg),
- a High Density Microarray platform (Ö. Türeci, III. Dept. of Internal Medicine),
- the Mass Spectrometry platform (H. Schild, Inst. of Immunology),
- a Flow Cytometry Core Facility as part of the Immunotherapy Center (A. Konur),
- an Imaging Center (R. Kiesslich, I. Dep. of Internal Medicine), and
- spin-off companies (http://www.ganymed-pharmaceuticals.de, http://www.thymed.de/).

On the basis of pre-existing activities the Medical Faculty formed a prioritized **Immunologic Diseases and Tumor Research Center** (Chapter 11.2, p 28).

Excellence in oncology-related research at the Johannes Gutenberg-University is demonstrated by outstanding contributions:

in basic and preclinical research	tumor antigen identification	Koslowski M., *Cancer Res.* 2004; Türeci Ö., *Methods Mol. Med.* 2004; Lennerz V., *PNAS* 2005
	immunoevasion and T cell regulation	Reddehase M., *Nat. Rev. Immunol.* 2002; Seliger B., *Trends Immunol.* 2003; Jonuleit H., *J. Exp. Med.* 2001; Bopp T., *J. Exp. Med.* 2005; Warger T., *Blood* 2006
	adoptive T cell transfer	Stanislawski T., *Nat. Immunol.* 2001; Kuball J., *Immunity* 2005; Dörrschuck A., *Blood* 2004
	tumor promotion and carcinogenesis	Becker C., *Immunity* 2004; Prawitt D., *PNAS* 2005; Bockamp E., *Blood* 2006
	susceptibility to cancer	Oesch-Bartlomowicz B., *PNAS* 2005

in clinical research, early trials	early detection and prevention of cancer	Kiesslich R., *Gastroenterology* 2004
	gene therapy	Schuler M., *J. Clin. Oncol.* 2001; Kuball J., *J. Clin. Oncol.* 2002
	tyrosine kinase inhibition	Kindler T., *Blood* 2004; Hess G., *J. Clin. Oncol.* 2005; Heidel F., *Blood* 2006
	epidemiology	Schuz J., *Am. J. Epidemiol.* 2006 Schilling F.H., *N. Engl. J. Med.* 2002

… within international study groups	acute myeloid leukemia	Lowenberg B., *N. Engl. J. Med.* 2003; van der Holt B., *Blood* 2005
	Chron. myeloid leukemia	Kantarjian H., *N. Engl. J. Med.* 2002; O´Brien S.G., *N. Engl. J. Med.* 2003
	infectious diseases	Ullmann A., *Clin. Infect. Dis.* 2006

8 Research projects / groups / laboratories

A high percentage of project leaders are physician scientists, who are members of ITC-associated DMGs. Regular interdisciplinary board meetings already proved very helpful in launching cooperative projects. Scientists from 25 institutions perform oncology-related research projects. Among these are

- combined research projects (http://www.sfb432.uni-mainz.de/; http://www.uni-mainz.de/FB/Medizin/MedMikro/; http://sfb548.hautklinik-mainz.de/de/index.htm; http://zope.verwaltung.uni-mainz.de/forschung/schwerpunkte/forschergruppen/show) located in Mainz, as well as national and international programs chaired by local scientists;

- biobanking initiatives; and

- graduate and postgraduate teaching & training programs (http://www.immuntherapie.uni-mainz.de/; http://www.neurogrk.medizin.uni-mainz.de/) initiated at the Johannes Gutenberg-University as well as a joint program of several clinical departments to support physician scientist curricula.

Synergy finding is particularly well documented for the *immunology research program*, to which scientists from several clinical departments and theoretical institutes contribute. Basic immunologists and clinical immunologists focusing on allergy, autoimmunity, infectious diseases or tumor immunology are project leaders in three local combined research groups, and are additionally supported by the Rhineland-Palatinate's Immunology Cluster of Excellence "Immunointervention" (http://www.ice-mainz.de/). Their interactions led to seminal work (Chapter 7, p 14) and paved the way towards successful translational research (**Figure 4**, p 16).

Bridging between basic and applied sciences in other research areas is demonstrated by the following examples:

- B. Kaina and colleagues (Institute of Toxicology) analyze basic DNA repair mechanisms in cellular defense against genotoxic and cytotoxic effects. They collaborate with clinical researchers in Internal Medicine, Dermatology, Neurosurgery and Radiation Oncology. The goals are to establish predictive assays, to determine the sensitivity of cells to anticancer drugs and to apply DNA repair inhibitors to sensitize tumors to anticancer drugs.

- T. Fischer and colleagues (III. Department of Internal Medicine), who therapeutically target oncogenic signaling, collaborate with H. Decker (Institute for Molecular Biophysics) and U. Meissner (Institute of Zoology) on the molecular modeling of mutated tyrosine kinase for structure-function analysis.

- Two *inter-faculty teaching and training programs* for graduate and postgraduate students involve members of the Faculty of Biology and the Faculty of Medicine.

Tissue banking initiatives, in part supported by integrated research programs, play a pivotal role in promoting these interactions.

Translation from bench to bedside is far advanced within the tumor immunology program. The identification of tumor-associated antigens recognized by antibodies and T cells is a long-term project performed with elaborate techniques by several local groups. They discovered cancer/germline (CG), lineage-specific, minor histocompatibility antigens as well as highly tumor-specific antigens carrying point mutations. Many of these molecules represent hitherto poorly characterized genes of unknown function. Target molecules are characterized and validated with respect to their immunogenicity, their expression pattern in normal and malignant tissues and their function. On the basis of these results they are chosen as candidates for immunotherapy. Distinct intervention strategies are pursued and are carried from animal experiments towards clinical application. Partnerships with Biotech Companies and research-driven pharmaceutical companies were entered. **Figure 4** summarizes this program and lists its key researchers.

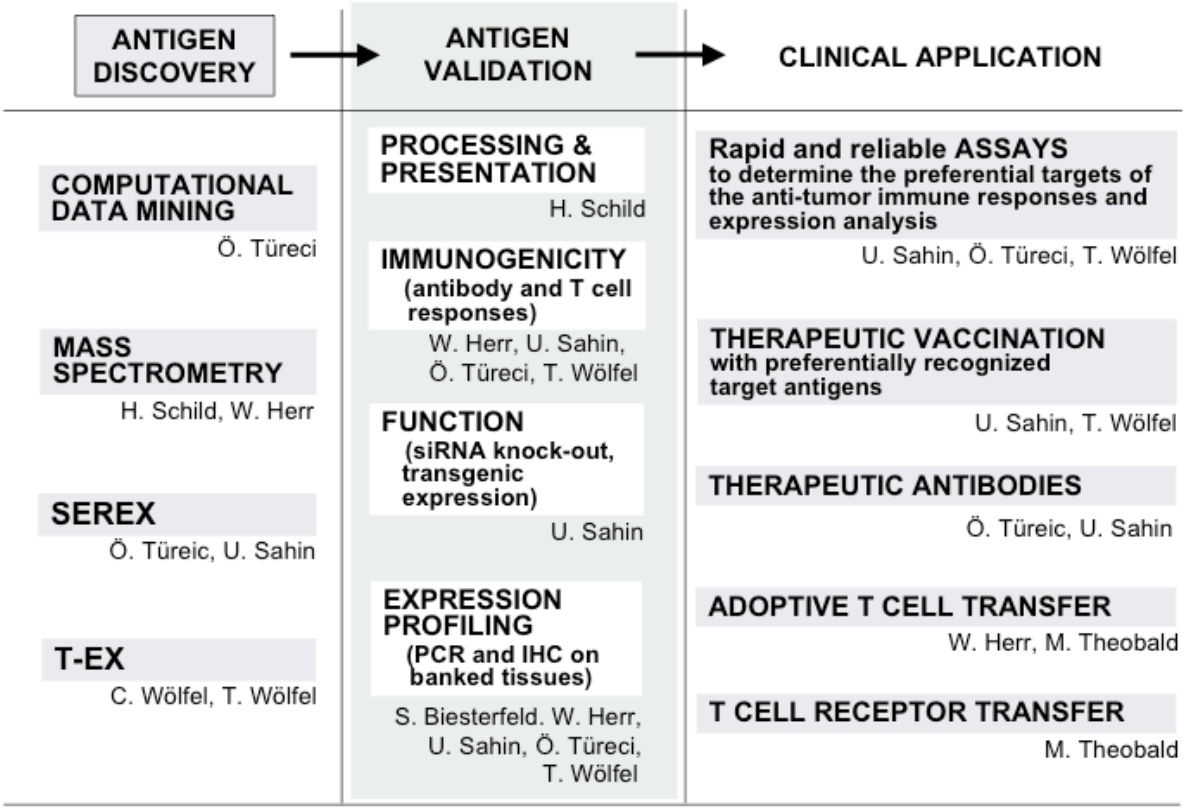

Figure 4: Translation from bench to bedside within the tumor immunology program.

9 Summary of future laboratory and clinical research topics

The ITC will promote

(1) the bridging of basic and clinical sciences,

(2) the involvement of surgical disciplines in combined research programs, and

(3) the implementation of innovative and investigator-initiated studies emanating from local research programs,

(4) the establishment of a comprehensive clinical cancer registry.

ad (1): examples

- The groups of M. Schmidt (Physical Chemistry), K. Mullen (Max Planck Institute for Polymer Research) together with U. Sahin (III. Dept. of Internal Medicine) will address the encapsulation of vaccine RNA (encoding antigens identified within the local antigen discovery program, see Figure 4, p 16) into nanocarriers to protect the RNA from degradation and to improve its immunopharmacological properties.
- G. Dannhardt (Institute for Pharmacy) and T. Fischer (III. Dept. of Internal Medicine) will jointly test the mechanisms of action of small molecule signal transduction inhibitors in cellular systems and angiogenesis models.

ad (2):

It will be a major challenge in oncology to identify manageable and reliable genetic and phenotypic markers for risk stratification and treatment susceptibility. Their relevance has been impressively demonstrated in lymphohemotopoetic malignancies. Analogous achievements in solid tumors will be an indispensable step towards the improvement of therapeutic efficacy and will also go along with a rational adaptation of therapy and aftercare to individual needs. Considering the variety of innovative treatment options this will certainly be cost-effective. Surgical oncologists are in a key position within a complex network of basic and clinical sciences and are therefore prime partners in combined research programs.

- Several of the surgical departments have initiated or contribute to biobanking, which is a major asset for networking to reach the above mentioned goals. The ITC will support quality assurance and mediate centralization.
- Surgical oncologists identify and treat patients with limited clinical disease, a significant proportion of whom is at a high risk of metastatic spread. Such patients are regarded as best candidates for immunotherapy. Project leaders forwarding immunotherapy approaches (see below) will therefore seek partnerships with surgical oncologists.
- E.g., neurosurgeons and neurologists together with other partners formed a Neurooncology disease management group, initiated and contributed to multicenter clinical trials and started to design laboratory projects. They find support by established oncological integrated research programs and also by the neuroscience network

"Molecular and Cellular Neurobiology" (http://www.iak-neuro.uni-mainz.de/index_eng.html) established at the Johannes Gutenberg-University.

ad (3): examples

- Within the tumor immunology program several therapeutic approaches were developed and carried from basic to preclinical research by ITC members and their partners (**Figure 4**, p 16). They are supported by the University's spin-off company Ganymed Pharmaceuticals AG (http://www.ganymed-pharmaceuticals.com/) and by additional links to external academic partners and to pharmaceutical industry. Phase I testing is planned within the next years for
    - the therapeutic vaccination with RNA encoding tumor-associated antigens (U. Sahin, III. Dep. of Internal Medicine),
    - an antibody recognizing an adenocarcinoma-associated antigen (Ö. Türeci, Ganymed Pharmaceuticals),
    - the retroviral transfer of T cell receptors with high avidity for tumor-associated antigens (M. Theobald, III. Dep. of Internal Medicine).
- M. Neurath and colleagues (I. Dep. of Internal Medicine) uncover the pathogenesis of colitis-associated colorectal cancer. This group is designing trials to prevent cancer development in patients with chronic inflammatory bowel diseases. Candidate agents are the histon deacetylase inhibitor sodium valproate as well as antibodies against IL-6R and TNF-a. This goes along with the same group's achievements in early GI cancer detection with miniaturized endoscopic systems and endomicroscopy, for which a developmental partnership was recently initiated with Johns Hopkins clinical researchers.

ad (4):

Clinical cancer registration is a highly important tool for quality management in cancer treatment. Registry data may be used for both clinical and epidemiological research. While such registration is performed at the Mainz University Hospital for single entities, it is a core issue for the ITC to help in establishing a comprehensive cancer registry for all patients that have been treated at the ITC Mainz (Chapter 12, p 30). Along these lines a second stage is planned to include analogous registries for other, non-academic Cancer Centers to be established in Rhineland-Palatinate.

Supplementary information on the infrastructural basis for future research and development:

While a CCC-equivalent structure would be instrumental to bring forward the integration and shaping of oncological research activities, the Faculty constantly takes measures to improve the **infrastructural basis for future research and development**.

A) Established activities are:

- the Faculty's Immunologic Diseases and Tumor Research Center funded with priority (Chapter 11.2, p 28), and
- a Coordinating Center of Clinical Studies (KKS, led by M. Seibert-Grafe) also hosting the Central Coordinating Unit of PAED-Net (Chapter 10.7, pp 24-25).

B) Funding applications have been launched within the following nationwide grant programs:

- „Interdisciplinary Center for Clinical Studies" (IZKS) of the BMBF (Bundesministerium für Bildung und Forschung) (Coordinators: F. Zepp, M. Seibert-Grafe),
- „*Excellence Initiative by the German Federal and State Governments to Promote Science and Research at German Universities*", Graduate School Program (Coordinator: M. Neurath),
- „*Excellence Initiative by the German Federal and State Governments to Promote Science and Research at German Universities*", Excellence Cluster Program (Coordinators: C. Huber, H. Schild),
- „*Integrated Research and Treatment Centers*" (IFB) of the BMBF (Bundesministerium für Bildung und Forschung) (Coordinators: C. Huber, P. Galle,).

These activities demonstrate that the Faculty is determined to support the translation of basic research into patient-oriented research and provide all the prerequisites needed to perform clinical studies according to modern standards. This will form a solid basis for the ITC efforts to include a substantially higher proportion of oncological patients, especially with solid tumors, into ICH-GCP-compliant studies. Aside from University-driven study initiatives, research-oriented pharmaceutical companies will more easily find partners to study innovative treatment concepts in a big variety of malignant diseases.

10 Clinical care

10.1 Size of the hospital

The hospital of the Johannes Gutenberg-University in Mainz is the only University Hospital in Rhineland-Palatinate. It is determined to provide approximately 4.1 Mio people with supramaximum medical care. More than 40 institutions form a center of referral and offer specialty care programs, but also help to cover the region's primary health care. In 2005 altogether 57,222 inpatients and 161,890 outpatients with a broad spectrum of diseases were treated in the hospital. Each year approximately 8,000 cancer patients have been cared for. About 4,000 new cancer patients are annually admitted to the Hospital.

Currently 2,808 medical students receive undergraduate medical education, and about 700 physicians and physician scientists are in training for postgraduate education and specialized medical care.

10.2 Numbers of newly diagnosed cancer patients in 2005

Approximately 4.000 newly diagnosed cancer patients have been cared for in 2005 at the University Hospital of Rhineland-Palatinate. This amounts to approximately 11% of all cancer patients reported to the epidemiologic Rhineland-Palatinate cancer registry:

ICD	**Cancer cases reported by the University Hospital to the Rhineland-Palatinate cancer registry in 2005**
Nervous system C47,C70-72,D32-33,D42-43	166
Head and neck C00-14	218
Esophagus C15	93
Stomach C16	95
Colon/rectum C18-21	262
Liver C22	207
Gallbladder and biliary tract C23-24	43
Pancreas C25	99
Larynx C32	47
Lung C33-C34	148
Bone/cartilage/other connect. & soft tissue C40,41,49	45
Skin (melanoma and others) C43-44	523
Breast, incl. carcinoma in situ C50-D05	240
Female genital organs, incl. in situ C51-57,D06,D07	125
Prostate C61	283
Testis C62	68
Urinary Tract, excl. bladder C64-C66 C68	154
Bladder C67 D09.0 D41.4	200
Thyroid gland C73	50
Lymphoma C81-C85	451
Multiple myeloma C90	127
Leukemia C91-C95	292
Total	**3936**

10.3 Integrated patient care, tumor boards

Entity-oriented centers and multidisciplinary disease management groups (DMG) meet weekly at regular hours in boards. Most of these boards are centrally organized by the ITC. A responsible coordinator (senior physician or Dept. Head) is assigned to each board. All patients to be discussed are announced in advance by case summaries, which are electronically distributed. Multidisciplinary approaches are discussed with all experts involved. Consensus recommendations are recorded in protocols sent out to all participants. Also private doctors and physicians from neighboring hospitals take advantage of discussing their patients with the board members, and, vice versa, experts of the University Hospital contribute to external boards on a regular basis. Centers, DMGs and tumor boards established to date at the University Hospital of Mainz and external boards, to which Faculty members regularly contribute (**Table I**).

Table I: Timetable of oncological tumor boards

Time	Monday	Tuesday	Wednesday	Thursday	Friday
8.00 am					G3: HCC
11.00 am					
11.30 am	G16$_{ext}$: Gyneco-Oncology (St. Vinzenz hospital)				
12.00 am					
12.30 pm			G13: Head + Neck I	G10: Neuro-Oncology	
1.00 pm					
1.30 pm		G5: Lung Cancer			
2.00 pm	G6: Stem Cell Transplant. G8: Gyneco-Oncology	G14: Head + Neck II	G4: General Interdiscipl. Oncology	G7: Breast Cancer	
2.30 pm					
3.00 pm					
3.30 pm				G11: GI Cancer G12: Soft Tissue Sarcoma	
4.00 pm	G17$_{ext}$: Lung Cancer (Hildegardis Hospital)			G9: Endocrine Cancer G15: Urology	
4.30 pm					

The DMGs are the central platforms for patient management, the establishment of internal guidelines, and the discussion of clinical studies, into which patients will be recruited. The DMGs participate in multicenter studies. They also can launch investigator-initiated studies. DMGs are further platforms for the communication of clinicians with scientists, interested in certain diseases or treatment strategies.

In breast cancer, gynecological cancer and lung cancer all cases are presented in tumor boards. This is not yet reached for other entities due to the lack of resources. One of the aims of this application is to guarantee for all patients, that their cases are reviewed by interdisciplinary tumor boards.

10.4 Quality Assessment

Measures to ensure **process quality** at the University Hospital for cancer patient care are as follows:

- the implementation of national and international guidelines for diagnosis, treatment and after care;
- the treatment of cancer patients in about 160 different national and international clinical trials in certified clinical trial centers, and
- the certification and accreditation of several tumor centers, clinical departments, institutions and laboratories.

Quality outcome programs to provide data to objectively compare hospital performances in tumor patient care have been installed in some medical departments, e.g.:

- outcome quality will be available for breast cancer patients by using ODSeasy – a software tool released in 2005 to compare follow-up data with other breast cancer centers in Germany;
- clinical outcome data from patients with gastrointestinal tumors are managed with the Gießen Tumor Documentation System (GTDS) (http://www.med.uni-giessen.de/akkk/gtds/);
- a clinical cancer registry for patients with lung cancer treated at the University Hospital is available;
- head and neck tumor patients are followed within a clinical registry of the German-Austrian-Swiss Working Party for Maxillofacial Tumors (DÖSAK, http://www.doesak.org/), and
- long term follow-up is also available for patients treated with stem cell or bone marrow transplantation.

The implementation of a comprehensive clinical cancer registry at the University Hospital – and later at other partner hospitals in Rhineland Palatinate – will assure quality outcome data for all tumor entities.

10.5 Palliative and psychosocial care

An **Interdisciplinary Center of Palliative Care** at the University Hospital of the Johannes-Gutenberg-University in Mainz was opened in December 2005. It includes an eight-bed ward equipped for the special needs of patients suffering from incurable advanced disease. It is run by a team of physicians, nurses, social workers, pastors, physical therapists and volunteers. Expert medical oncologists, anesthesiologists and neurologists provide a consultative service both to outpatients and inpatients (to be named: M. Weber, Assistant Professor in Palliative Medicine; J. Jage, Associate Professor in Anesthesiology). They are also involved in teaching (contributing to mandatory units and offering optional seminars) and in regular continuing education. Moreover, they are members in the IST (interdisciplinary pain management program, see http://www-klinik.uni-mainz.de/Neurologie/). The Interdisciplinary Center of Palliative Care is closely connected with the regional palliative homecare team and the regional eight-bed inpatient hospice (Christopherus-Hospice in Mainz-Drais, http://www.caritas-werk-st-martin.de/christophorus-ho.html) as well as with the corresponding super-regional Hospice Working Group of Rhineland-Palatinate.

Psycho-oncological and psychosocial care is an integral part of the oncology service at the Mainz University Hospital. It is traditionally provided as a service by the Tumorzentrum Rhineland-Palatinate e.V. (http://info.imsd.uni-mainz.de/TUZ/; representative: Dr. med. A. Werner) and by the Dept. of Psychosomatic Medicine and Psychotherapy (Chairman and Head: E, Beutel). It includes:

- identification of social and psychological distress of patients and family members (screening questionnaires: HADS, EORTC, DISTRESS, POBADO);
- information, consultation and support of patients and their relatives (including crisis intervention);
- regular participation in rounds and staff meetings as well as team supervision in Hematology / Oncology, Blood Stem Cell Transplantation, Breast Cancer and Palliative Care Units; for all other units and Tumor Boards on demand;
- continuing education and training of internal and external staff members, and
- cooperation and networking between specialized services and institutions.

10.6 Documentation, clinical cancer registry, long term follow up

A) Electronic Health Record

The University Hospital of Mainz started the implementation of an electronic health record system (EHR) in September 2003. The platform, that has been chosen, is i.s.h.med (GSG Berlin, Germany), a SAP-based application, which interacts seamlessly with our hospital information system IS-H (SAP Walldorf, Germany). To date central functions like laboratory, radiology, operating room management, administration including DRG-management are campus-wide online. Further functions like digital archive and medical record management are under construction. The in-depth implementation of EHR is one of the main goals of the Hospital's Executive Board: last year the Hospital invested an additional 2.3 Mio € to accelerate the EHR development.

B) Clinical cancer registry and long term follow-up

Cancer registries for certain disease entities are implemented at the University Hospital or via external networking registries. Examples are given in Chapter 10.4, pp 21-22.

The Faculty's Institute for Medical Biometry, Epidemiology and Informatics (IMBEI) conducts both the Epidemiologic Cancer Registry of Rhineland-Palatinate and the German Childhood Cancer Registry (GCCR). The renowned epidemiologic and clinical GCCR is active since 1980 and currently contains 35,367 cases collected from a population of 13 Mio children.

Clinical data obtained within single entity registries will be matched with the large epidemiologic data pool of the Rhineland-Palatinate Cancer Registry.

The ITC will be instrumental to mediate the cross-linking of existing clinical cancer registries with the Rhineland-Palatinate Cancer registry and to establish a comprehensive clinical cancer registry with long-term follow up data for all cancer patients newly diagnosed at the University Hospital (Chapter 12, p 30). This process will enormously profit from the experience and infrastructure built up with the large IMBEI registries mentioned above.

10.7 Clinical trial center

About 160 clinical trials were open to cancer patients in the year 2005. Approximately 30% of them have been phase I and phase II trials. There is a large expertise in the oncological clinical research units to manage these complex trials. They address the complete spectrum of innovative approaches including therapeutic vaccination, antibody therapy, hematopoetic stem cell transplantation, anti-angiogenesis and signal transduction inhibition. In 2005, more than 2,000 clinical trial cancer patients visited the Hospital. In adults, approximately 27% of the patients with solid tumors and approximately 41% of patients with lymphohematopoetic malignancies were included in trials. Clearly, most of these trials exclude the rather large cohort of elderly patients with co-morbidities. This will certainly improve with the advent of appropriate studies for the elderly. In children, the fraction of patients in trials was 91% for lymphohemotopoetic neoplasms and 63% for solid tumors.

A series of single institutional and interdisciplinary centers and network programs at the Medical Faculty of the Johannes Gutenberg-University perform and/or coordinate these clinical trials. They are described in the following (A-D).

A) The Coordination Center of Clinical Studies (KKS)

The KKS (http://www.kks-mainz.de/) is an integral part of the Faculty of Medicine. It serves as the "Center of Competence" for clinical research at the University Hospital. Its agenda is to coordinate clinical research, which is conducted at the various Hospital Departments, and to provide personnel and resources for specific clinical research projects. The KKS is staffed with administrators, data managers, statisticians, study nurses and monitors. It is directed by Dr. M. Seibert-Grafe. Its advisory board consists of scientists of the Medical Faculty and external experts. It is planned to continue the KKS as „Interdisciplinary Center for Clinical Studies" (IZKS) with funding support from the BMBF (Ministry of Science of the Federal Government) (Chapter 9, p 19).

B) The Institutional and Disease-oriented Clinical Research Units

Several Departments host established clinical research units, which are devoted to conducting disease-specific clinical trials. These are

- the *Clinical Trial Center* of the I. Medizinische Klinik (http://www.klinik.uni-mainz.de/1-Med/) focussing on Gastrointestinal Oncology;
- the *Study Center Hematology/Oncology* at the III. Medizinische Klinik (http://www.3-med.medizin.uni-mainz.de/3Med/Studienzentrale/sz_index.html) conducting clinical studies in patients with lymphomas, leukemias, myeloma, breast cancer, lung urogenital and other cancers, and infectious complications;
- the certified *Hematopoetic Stem Cell Transplantation Unit* (http://www.3-med.medizin.uni-mainz.de/transplantation/javascript/index.html) together with its *GMP Cell Laboratory*; http://www.3-med.medizin.uni-mainz.de/3Med/AufgabenStrukturenIndex.html) conducting hematopoetic stem cell transplantation in leukemia, lymphoma and renal cell cancer;
- the certified *Breast Cancer Center* at the Department of Gynecology (http://www-klinik.uni-mainz.de/brustzentrum) for the multidisciplinary treatment of breast cancer, and
- the *Clinical Research Center* of the Department of Dermatology studying immune interventions in patients with skin cancers (see http://www.hautklinik-mainz.de/).

C) The PAED-Net

The PAED-Net (http://www.paed-net.org/) is a national network of six academic Departments of Pediatrics, which jointly perform multicentric clinical studies in pediatric patients. The Central Coordinating Unit of PAED-Net is hosted by the KKS Mainz. Services of the PAED-Net include protocol development, recruitment of qualified study centers, providing study personnel and resources, data collection, management and archiving, and public relations issues.

D) Institute of Medical Biometry, Epidemiology and Informatics (IMBEI)

The Institute (http://www.imsd.uni-mainz.de/) consists of the Departments for Biometry, Informatics and Epidemiology. The Department of Biometry provides statistical support for many different methodological questions and collaborates closely with the KKS. The Department of Informatics cooperates with the IT group on projects in clinical data processing and communication. The group has a unique experience in cryptography and data security and plays a leading role in developing models for data protection in medical research. Within the Department of Epidemiology there is a clear focus on research in cancer epidemiology and radiation epidemiology. The group has an immense expertise in population based studies and field work and has set up collaborations with different public health organizations. In addition, the IMBEI hosts the population-based Cancer Registry of the State Rhineland-Palatinate (since 1997), and the population-based German childhood Cancer Registry (since 1980) (Chapter 10.6 B, p 23). The IMBEI is determined to run a comprehensive Clinical Cancer Registry supported by the ITC Mainz.

10.8 Documentation of attempts to establish a stable interaction with local oncologists and hospitals

Active and permanent outreach programs have been initiated and developed by all of the ITC-related institutions, integrated projects and DMGs

- to strengthen the interaction in patient care,
- to provide certified continuing medical education for health care professionals in Rhineland-Palatinate, Saarland and Southern Hesse
- to promote scientific training and interactions.

ITC members organize certified scientific symposia as well as educational and updating meetings. Private doctors and clinicians from regional hospitals regularly contribute to ITC tumor boards. Exemplarily mentioned are the following permanent programs:

- regional Society of Medical Oncology (AIO) meetings (3 to 4 each year) covering a wide range of oncological subjects since more than 10 years (program director: T. Wölfel);
- post ASCO updates;
- annual international symposia of the Association for Immunotherapy of Cancer since 2003 (http://www.c-imt.org/) (program directors: T. Wölfel, S. Kreiter, C. Britten, C. Huber), and
- from 2006 annual educational meetings in Mainz on the “Clinical Application of Cancer Immunotherapy” within the German-speaking program of the European School of Oncology (ESO-D) (program directors: T. Wölfel/Mainz, T. Cerny/St.Gallen, Ch. Zielinski/Wien, A. Knuth/Zürich) (http://www.c-imt.org/).

As mentioned in Chapter 10.5 (p 22), the Interdisciplinary Center of Palliative Care is closely connected to the regional palliative homecare team and the regional eight-bed inpatient hospice (located in Mainz-Drais) as well as with the corresponding super-regional Hospice Working Group of Rhineland-Palatinate.

The *Tumorzentrum Rheinland-Pfalz e.V.*, located in the immediate neighborhood of the University Hospital, maintains a complementary educational program for health professionals in Rhineland-Palatinate (http://info.imsd.uni-mainz.de/TUZ/).

11 Local Funding for the Cancer Center

11.1 Core-structure and Core-activities of the ITC

Table II lists the **core personnel** with full-time commitment to the ITC and their function according to its organizational structure (**Figure 1**, p 9).

Table II: Full-time core personnel of the ITC Mainz

Name	Position	Affiliation / Wage level	Function within ITC
Thomas Wölfel, Dr. med.	Assoc. Prof.	(1) / C3	Cancer Center Director
Ute Kreiter, Dr. med.	Clin. Assoc.	(1) / BAT Ib/2	administrative management
Kristiane Preuss	Assistant	(2) / BAT Vc/b	assistance to all management activities, organization of tumor boards and their reporting, organization of meetings and symposia

(1) staff members of the III. Dept. of Internal Medicine (Hematology/Oncology, Dir.: Ch. Huber)
(2) private donation (administrated by III. Dept. of Internal Medicine)

One of the major investments of the recent years is a central building (building 605) for all internal medicine departments. It will be functional in fall 2006. **Building 403** can then be made available to the ITC to accommodate its core activities including a centralized outpatient clinic, where systemic chemotherapy by ITC partners will also be performed. This building (ground and 1st floor) was renovated only two years ago to temporarily accommodate the outpatient clinic of the III. Department of Internal Medicine with its hematopoetic stem cell transplantation unit and is therefore appropriately equipped. **Figure 2** (p 9) shows the exterior view of Building 403.

The personnel of the interdisciplinary ambulance will be composed of:

- 3,25 attending physicians (BAT Ib),
- 5 physicians in training (BAT IIa),
- 7 nurses (BAT Va).

They are affiliated to the I. and III. Departments of Internal Medicine and to the Departments of Gynecology, Radiation Oncology, Neurology and Neurosurgery.

Currently, thirteen **tumor boards** are held within the University Hospital on a weekly basis (**Table I**, p 21). Each board is on average run by three to four clinical experts from distinct specialties (Attending Physicians, Department Heads) in addition to case presenters. Personnel involved in board organization, case discussion, reaching agreement on recommendations to primary caregivers as well writing and distributing the protocols is at present equivalent to

- 1.5 attending physicians (BAT Ia/b);
- 3 physicians in training (BAT IIa), and
- 1 secretary (BAT Vb,c).

11.2 Funding of Oncological Research Programs

External funding for oncology-related research at the Johannes Gutenberg-University sums up to approximately **27 Mio EUR** in the past 3 years.

Intramural funding by Medical Faculty prioritizes four research centers, all of which relate to oncological research and development (http://dekanat.medizin.uni-mainz.de/Aktuelles/aktuelles.html). These are:

- the Immunologic Diseases and Tumor Research Center,
- the Neuroscience Research Center,
- the Preventive Medicine Research Center, and
- the Minimal Invasive Surgery Research Center.

These Research Centers have approximately **0.5 Mio EUR** each year at their disposal. In addition, an intramural funding program (MAIFOR) annually supports scientists working in these fields with approximately **2 Mio EUR**.

Beginning in 2005, the **State Government of Rhineland-Palatinate** supports the infrastructure of immunological research by funding the Immunology Cluster of Excellence (ICE) “Immunointervention” with **1.7 Mio EUR** each year. About half of the projects are oncology-related. The first funding period will end in 2007. The Government has already announced that it will continue the program.

The commitment of the Johannes Gutenberg-University to sustain its status as a research-oriented university is exemplified by the investment of **23 Mio EUR** by the State Government to build a new central animal facility.

12 Summary

The hospital of the single Medical Faculty in Rhineland-Palatinate is an integral part of the Johannes Gutenberg-University in Mainz. About 4,000 new cancer patients are annually admitted to the Hospital. In 2003 the development of an interdisciplinary tumor center (ITC Mainz) was initiated by faculty members. Aims were to improve standard patient care throughout the large field of oncology, to put into effect the promises made by exponentially evolving treatment options and to synergize a multitude of pre-existing research activities and study programs. The latter is exemplified by the faculty's cancer immunology program.

Within the ITC frame a certified breast cancer center was established in 2004, as well as trans-institutional disease management groups (DMGs) with weekly tumor boards for other disease entities such as lung, gastro-intestinal, head-and-neck, lymphohematopoetic, endocrine, mesenchymal and central nervous system neoplasms. A central interdisciplinary outpatient clinic is determined to open in fall 2006. Psycho-oncological counseling and interdisciplinary palliative care are implemented. With respect to teaching, training and continuing education

- multidisciplinary oncology lectures were initiated to provide a systematic medical oncology curriculum to medical students,
- the curricula of physician scientists are specifically supported,
- graduate and postgraduate students in Medicine and Biology are offered to join interfacultary research training groups and international Master Programs, and
- active and permanent outreach programs for health care professionals have been developed.

The University's Medical Faculty strongly supports preclinical and clinical research in oncology together with the scientific infrastructure for the planning, performance, and assessment of clinical studies.

Future developments aim

- to guarantee all patients´ cases to be reviewed by an interdisciplinary tumor board, and
- to promote clinical scientific research activities for all disease entities treated in Mainz *by establishing further DMGs and sustaining their organization and performance*,
- to include a substantially higher proportion of oncological patients into ICH-GCP-compliant studies *by the initiation and acquisition of pivotal clinical studies in early and late phases for a larger variety of cancer types*,
- to ascertain and improve quality management in cancer treatment *by establishing a comprehensive clinical cancer registry*, and
- to improve the outreach *by extending teaching, training and continued medical education activities.*