Riferimento a linee guida	SCHEDA N: 4 AUTOVALUTAZIONE PROGRAMMA
3	Nome programma:
	Molecular and cellular target involved in the drug activity
3	Responsabile programma
	Francesco Dall'Acqua
3	Obiettivi specifici del programma
	The mechanism of pharmacological action of various molecules is studied utilizing different *in vitro* experimental models, in particular cell cultures. The potential targets at cellular and biomolecular level is also analysed with different biological assays.
3	Progetti in corso
	Project 1: New photonucleases containing the quinolizinium ion. Evaluation of the DNA-binding and DNA-photocleaving properties. *Project 2: Photopheresis and PUVA therapy: study of the mechanism of action of psoralen derivatives.* Analysis of the mechanism leading to photoinduced cell death in different cell types such as human lymphocytes, monocytes and keratinocytes. *Project 3: Analysis of the photostability and phototoxicity of drugs.* Studies of drug photostability in aqueous solution and in their pharmaceutical preparations. Evaluation of in vitro phototoxicity at cellular and biomolecular level. *Project 4: New potential antitumor and photochemotherapeutic drugs.* Evaluation of antiproliferative activity and their mechanism of action in a panel of human tumor cell lines. *Project 5:* Study of the photoinduced erhythroid differentiation with psoralen in human myeloid leukaemia cells (K562) as experimental model and in stem cells from human health volunteer.
4.b	Risorse personale
	Prof. Francesco Dall'Acqua (Full Professor) Prof. Daniela Vedaldi (Full Professor) Prof. Sergio Caffieri (Associate Professor) Prof. Giorgia Miolo (Assistant Professor) Dr. Giampietro Viola (Technician) Dr. Anita Faccio (PhD student) Dr. Federica Gallocchio (PhD student) Dr. Alessia Salvador (PhD student)
5.b	Risorse finanziarie [media quinquennale]
	In the period 2001-2005, the program received through the Department a mean of € 63000 per year. Moreover, some researchers were involved in projects that were funded by external organisations.
7	Rapporti con altri istituti di ricerca a livello locale, nazionale e internazionale
7.a	In the frame of PRINs, the research group coworked with the Depts of Chemistry of the Universities of Perugia (Prof. Ugo Mazzucato) and Pavia (Prof. Elisa Fasani) and with the Dept of Biology of the University of Padova (Dott. Elena Reddi). The network also

	comprehended the Depts of Chemistry of the Universities of Padova, Catania and Modena. Department of Pediatrics, Clinica oncoematologica, Università di Padova (Prof. Giuseppe Basso)
7.b	Department of Organic Chemistry, University of Siegen (D) (Prof. H. Himmels) Pharmacochemical Department, University of Palermo (Prof. G. Cirrincione) Department of Organic Chemistry, University of Firenze (Prof. S. Chimichi) Department of Biochemistry and Molecular Biology, University of Ferrara (Prof. R. Gambari) Department of Pharmacology and Anesthesiology, Medical School, University of Padova (Prof. P.Giusti). Center for Medicinal Photochemistry, University of Leiden (NL) (Prof. G.M.J. Beijersbergen van Henegouwen)
9	Altre attività rilevanti per la ricerca, a livello di Programma
	Collaboration to congress and symposium organization Organization of the 3rd Convegno Congiunto di Fotobiologia e Fotochimica. Padova, 6-8 giugno 2002 (Caffieri). Organization of the session “Psoralens” at the 10th Congress of the European Society for Photobiology, Vienna 6-11 September 2003 (Dall’Acqua) **Congresses attended** 2001: 7 2002: 10 2003: 9 2004: 5 2005: 8
11	Prodotti della ricerca
11.b	**Articles** **2001** H. Ihmels, K. Faulhaber, C. Sturm, G. Bringmann, K. Messer, N. Gabellini, D. Vedaldi, G. Viola. Acridizinium salts as a novel class of DNA-binding and site-selective DNA-photodamaging chromophores. *Photochem. Photobiol.* **74**, 505-511 (2001). IF 2.054. S. Caffieri, RP-HPLC determination of lipophilicity of furocoumarins. Relationship with DNA interaction. *J. Pharm. Sci.*, **90**, 732-739 (2001). IF 2.180 A. Chilin, P. Manzini, S. Caffieri, P. Rodighiero, A. Guiotto, Difurocoumarins: psoralen analogs as photochemotherapeutic agents. *J. Heterocycl. Chem*. **38**, 431-434 (2001). IF 0.814 H. Ihmels, K. Faulhaber, K. Wissel, G. Bringmann, K. Messer, G. Viola, D. Vedaldi. Synthesis and investigation of the DNA-binding and DNA-photodamaging properties of indolo[2,3-*b*]quinolizinium bromide. *Eur. J. Org. Chem.* **6**, 1157-1161 (2001). IF 2.426 **2002** M. Borges, A. Romao, O. Matos, C. Marzano, S. Caffieri, R.S. Becker, A.L. Maçanita, Photobiological properties of hydroxy substituted flavothiones. *Photochem. Photobiol*.

	75, 97-106 (2002). IF 2.054 S. Caffieri, Furocoumarin photolysis: chemical and biological aspects. Photochem. Photobiol. Sci. **1**, 149-157 (2002). IF 1.798 M. Canton, S. Caffieri, F. Dall'Acqua, F. Di Lisa, PUVA-induced apoptosis involves mitochondrial dysfunction caused by the opening of the permeability transition pore. *FEBS Letters* **522**, 168-172 (2002). IF 3.843 S. Chimichi, M. Boccalini, B. Cosimelli, G. Viola, D. Vedaldi, F. Dall'Acqua. New geiparvarin analogues from 7-(2-oxoethoxy)coumarins as efficient in vitro antitumoral agents. *Tetrahedron Letters* **43**, 7473-7476 (2002). IF 2.484 S. Chimichi, M. Boccalini, B. Cosimelli, G. Viola, D. Vedaldi, F. Dall'Acqua. A convenient synthesis of psoralen. *Tetrahedron* **58**, 4859-4863 (2002). IF 2.643 F. Eisei, L. Latterini, G.G. Aloisi, U. Mazzucato, G. Viola, G. Miolo, D. Vedaldi, F. Dall'Acqua. Excited-state properties and in vitro phototoxicity studies of three phenothiazine derivatives. *Photochem. Photobiol.* **75**, 11-21 (2002). IF 2.054 G. Miolo, S. Caffieri, L. Levorato, M. Imbesi. P. Giusti, T. Uz, R. Manev, H. Manev, Photoisomerization of fluvoxamine generates an isomer that has reduced activity on the 5-HT transporter and does not affect cell proliferation. *Eur. J. Pharmacol.*, **450**, 223-229 (2002). IF 2.432 G. Miolo, G. Viola, D. Vedaldi F. Dall'Acqua, A. Fravolini, O. Tabarrini, V. Cecchetti. In vitro phototoxic properties of new 6-desfluoro and 6-fluoro 8-methyl quinolones. *Toxicology in vitro* **16**, 683-93 (2002). IF 1.464 G. Viola, M. Bressanini, N. Gabellini, D. Vedaldi, F. Dall'Acqua, H. Ihmels. Naphthoquinolizinium derivatives as a novel platform for DNA-binding and DNA-photodamaging chromophores. *Photochem. Photobiol. Sci*. **1**, 882-889 (2002). IF 1.798 G. Viola, F. Dall'Acqua, N. Gabellini, S. Moro, D. Vedaldi, H. Ihmels. Indolo[2,3-b]-quinolizinium bromide: an efficient intercalator with DNA-photodamaging properties. *ChemBioChem* **3**, 550-558 (2002). IF 3.474. **2003** P. Barraja, P. Diana, A. Lauria, A. Montalbano, A.M. Almerico, G. Dattolo, G. Cirrincione, G. Viola, F. Dall'Acqua. Pyrrolo[2,3-h]quinolinones: synthesis and photochemotherapic activity. *Bioorg. Med. Chem. Lett*. **13**, 2809-2811 (2003). IF 2.333 S. Chimichi, M. Boccalini, B. Cosimelli, F. Dall'Acqua, G. Viola. New 5 – (2-ethenylsubstituted)–3(2H)–furanones with in vitro antiproliferative activity. *Tetrahedron* **59**, 5215-5223 (2003). IF 2.643 H. Ihmels, K. Faulhaber, K. Wissel, G. Viola, D. Vedaldi. 6-Aminoacridizinum bromide: a fluorescence probe which lights up in AT-rich regions of DNA. *Org.*

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Patents

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	Viola, Farmaco per la cura della talassemia, dell'anemia falciforme e di tutte le altre forme di anemia trattabili con questo, metodo di attivazione del farmaco, composizione farmaceutica avente come principio attivo il farmaco e metodo fotochemioterapico utilizzante il farmaco. Patent application N. VE2005A000054, registered 04/11/05
11.c	1. S. Chimichi, M. Boccalini, B. Cosimelli, G. Viola, D. Vedaldi, F. Dall'Acqua. New geiparvarin analogues from 7-(2-oxoethoxy)coumarins as efficient in vitro antitumoral agents. *Tetrahedron Letters* **43**, 7473-7476 (2002). IF 2.484 2. M. Canton, S. Caffieri, F. Dall'Acqua, F. Di Lisa. PUVA-induced apoptosis involves mitochondrial dysfunction caused by the opening of the permeability transition pore. *FEBS Letters* **522**, 168-172 (2002). IF 3.843 3. M. Schmittel, G. Viola, F. Dall'Acqua, G. Morbach. A novel concept to activate enediynes for DNA cleavage. *Chem.-Commun.* **5**, 646-647 (2003). IF 3.997 4. C. Bastianon, R. Zanoni, G. Miolo, S. Caffieri, E. Reddi, Mitochondria and plasma membrane as targets of the UVA-induced toxicity of some neuroleptic drugs: fluphenazine, perphenazine and thioridazine. *Int. J. Biochem. Cell Biol.* **37**, 901-908 (2005). IF 3.578 5. G. Viola, L. Facciolo, D. Vedaldi, S. Disarò, G. Basso, F. Dall'Acqua. Differential response of linear and angular psoralens in PUVA-induced apoptosis in HL-60 cells. *Photochem. Photobiol. Sci.* **3**, 237-239 (2004). IF 1.798
12	SWOT Analysis
	Strenghts One of the most important aspects of our programme concerns the fact that it has a strong interdisciplinary character, evidenced by the different scientific competences present in the research group. The arguments developed in the programme concern the mechanism of action of drugs studied at cellular, subcellular and biomolecular level. This multidisciplinary approach led to a deep knowledge of the basic mechanisms of different drugs, and this fact may be useful for the design and synthesis of new compounds endowed with better pharmacological and toxicological profiles. The obtained results have made it possible to explain, at a cellular level, f the mechanism of action of photopheresis, a clinical treatment used in the therapy of some type of tumors and immunological diseases. Moreover, encouraging results have recently been obtained, which suggest promising clinical application of some psoralens for the pharmacological treatment of β-thalassemia and other haematological disorders. **Weaknesses** The difficulty of involving young scientist experienced in the various aspects of this multidisciplinary programme, may represent a serious problem for the development of the different projects carried out by our research group. Furthermore, the involvement of expert technicians giving an important contribution to the experimental development of the research is also rather poor. **Opportunities** The programme, having a multidisciplinary character as well as potential clinical applications, represents an important opportunity even in the field of clinical therapy. **Threats** Teaching and examinations are official duty of Professors and Assistant Professors and take a large part of their time, reducing the time devoted to research.