Off-pump Coronary Artery Bypass Grafting: Single Center Experience with 1,000 Consecutive Patients

Oren Lev-Ran MD, Dmitri Pevni MD, Nahum Nesher MD, Ram Sharony MD, Yosef Paz MD, Amir Kramer MD, Rephael Mohr MD and Gideon Uretzky MD

Department of Cardiothoracic Surgery, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
Affiliated to Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

Key words: off-pump coronary artery bypass grafting, arterial conduits, no-touch aorta

Abstract

Background: Advances in surgical techniques and retractor-stabilizer devices allowing access to all coronary segments have resulted in increased interest in off-pump coronary artery bypass. The residual motion in the anastomotic site and potential hemodynamic derangements, however, render this operation technically more demanding.

Objectives: To evaluate the OPCAB experience in a single Israeli center.

Methods: Between 2000 and 2003 in our institution, 1,000 patients underwent off-pump operations. Patients were grouped by the type of procedure, i.e., minimally invasive direct coronary artery bypass or mid-sternotomy OPCAB.

Results: One hundred MIDCAB operations were performed. Of the 900 OPCAB, 767 patients received multiple grafts with an average of 2.6 $\pm$ 0.6 grafts per patient (range 2–4) and the remaining patients underwent single grafting during hybrid or emergency procedures. In the multiple-graft OPCAB group, complete revascularization was achieved in 96%. Multiple arterial conduits were used in 76% of the patients, and total arterial revascularization without aortic manipulation, using T-graft (35%) or *in situ* configurations, was performed in 61%. The respective rates for early mortality, myocardial infarction and stroke in the MIDCAB were 1%, 0% and 2%, and 2%, 1.3% and 0.9% in the multiple-vessel OPCAB groups. Multivariate analysis identified renal dysfunction (odds ratio 11.5, confidence interval 3.02–43.8; $P <$ 0.0001) and emergency operation (OR 8.74, CL 1.99–38.3; $P =$ 0.004) as predictors of mortality. The proportion of off-pump procedures increased from 9% prior to the study period to 59%.

Conclusions: The use of OPCAB does not compromise the ability to achieve complete myocardial revascularization. Our procedure of choice is OPCAB using arterial conduits, preferably the 'no-touch' aorta technique.

IMAJ 2004;6:665–669

For Editorial see page 695

Coronary artery bypass grafting plays a central role in the management of patients with ischemic heart disease. For more than three decades, surgeons have used cardiopulmonary bypass to provide a still and bloodless field in which to accomplish optimal anastomoses. Over time, changing demographics have led to a higher proportion of older and sicker patients referred for surgical revascularization [1]. There has been concern that these patients may not tolerate cardiopulmonary bypass [2]. If it could be done safely, avoiding exposure to the cardiopulmonary bypass may provide safer surgical revascularization in higher risk patients [3–6]. In recent years, advances in retractor-stabilizer systems, cardiac positioning devices, and operative techniques allow access to all coronary artery segments on the displaced beating heart. Subsequently, there has been increased interest in the off-pump coronary artery bypass [7].

In the past few years there has been a significant increase worldwide in the number of cardiac centers that have adopted OPCAB [3–8]. At the Tel Aviv Sourasky Medical Center we began to perform off-pump coronary surgery on a routine basis in September 2000. We report our experience with minimally invasive direct coronary artery bypass and OPCAB strategies with and without aortic manipulation.

Patients and Methods

Study design

Between September 2000 and September 2003, 1,000 consecutive patients underwent off-pump coronary revascularization. For the analysis, we excluded patients undergoing conventional on-pump coronary artery bypass grafting or combined procedures. The study group comprised all patients undergoing isolated off-pump coronary bypass procedures during the study period.

The following data were recorded prospectively for all patients: age, gender, height, weight, cardiac catheterization results (degree of left main coronary artery stenosis, total number of significantly diseased coronary arteries, left ventricular end-diastolic pressure, and ejection fraction), prior CABG operation, co-morbid conditions (diabetes, peripheral vascular disease, renal failure, chronic obstructive pulmonary disease), preoperative intraaortic balloon pump, date of operation, priority of operation (emergent, urgent, or

OPCAB = off-pump coronary artery bypass
MIDCAB = minimally invasive direct coronary artery bypass
OR = odds ratio
CI = confidence interval

CABG = coronary artery bypass grafting

elective), and the in-hospital outcomes of intraoperative or postoperative use of an IABP, intraoperative or postoperative stroke, reoperation for bleeding, sternal wound infection or dehiscence requiring operation, postoperative atrial fibrillation, date of discharge, and status at hospital discharge.

All patients were routinely screened by carotid Doppler assessments. The patients who required carotid endarterectomy, i.e., symptomatic with unilateral stenosis >70% or symptomatic with severe bilateral stenosis, were excluded from this study.

Definition of terms

Patients' data were collected and analyzed according to the STS National Cardiac Surgery database guidelines and definitions (http://www.ctsnet.org/doc/4314). Early mortality was defined as death occurring within 30 days of the operation. Stroke was defined as global or focal neurologic deficit that was evident after emergence from anesthesia and categorized as either permanent or reversible (transient ischemic attacks and prolonged reversible ischemic neurologic deficit). All neurologic events were evaluated by a neurologist and further confirmed by computed tomographic scan. Deep sternal wound infection was defined as a sternal infection requiring antibiotic agents and re-operation for sternal debridement. Incomplete revascularization was defined as the failure to graft one coronary artery of >1 mm in diameter that was preoperatively planned for grafting.

Surgical technique and postoperative management

MIDCAB operations were performed through a small left anterior thoracotomy, using a designated stabilizer (Cardio-Thoracic Systems, USA) and were limited to a single graft, i.e., the left internal thoracic artery to the left anterior descending artery. All OPCAB operations were performed through a midline sternotomy. Anticoagulation was achieved using 2 mg/kg of heparin and the activated clotting time was maintained above 300 seconds. The heart was stabilized using a suction tissue stabilization system (Octopus, Medtronic Inc, USA). A deep pericardial retraction suture was placed at the posterior fibrous pericardium medial to the proximal part of the inferior vena cava to help manipulate and rotate the heart to vertical and lateral positions. Vessel occlusion was achieved by external encircling silicone rubber bands. Intracoronary shunts were used occasionally.

The choice of conduits and configuration was made by the operating surgeon and was based on technical considerations described previously [9]. The use of bilateral ITA was generally avoided in patients with chronic obstructive pulmonary disease, emergency operations, female gender with body mass index of 30 kg/m^2 or more, and the subset of insulin-treated diabetic patients [9]. Grafting in the no-touch subgroup consisted of arterial conduits only. These included the left and right internal thoracic artery, the radial artery and the right gastroepiploic artery. The grafts were deployed in the following configuration: a) *in situ* left-sided bilateral ITA, and b) T-grafts constructed of bilateral ITA or left ITA and radial artery. The ITAs were routinely skeletonized [9] and dissection of the RA and the RGEA was facilitated by ultrasonic scalpel (Harmonic Scalpel, Ethicon Endosurgery, USA). The choice of configuration was determined by technical considerations related to the conduits, as has been previously described for conventional on-pump CABG [9]. All saphenous vein grafts were attached to the aorta and constructed proximally after placement of a partial aortic clamp. Anterior wall revascularization was routinely performed first in the sequence of grafting in both groups.

Postoperatively, all patients received intravenously administered isosorbide dinitrate (4–20 mg/hr) for 2 days. Oral calcium blockers (Dilatam®, Teva, Israel) were given to patients who received RA or RGEA conduits and continued for 6 months. Antiplatelet therapy included aspirin 250 mg per day (recommended for indefinite use) and clopidogrel 75 mg/day (Plavix®, Sanofi Winthrop, France) for 6 weeks postoperatively.

Statistical analysis

Univariate analysis involving chi-square tests for categorical variables and non-parametric tests for continuous variables were performed to assess the statistical significance of observed differences in patient characteristics between OPCAB subgroups. Logistic regression was used to evaluate the effect of preoperative and intraoperative descriptors on occurrence of early mortality. Covariates in the multivariate analyses included: age, gender, body mass index, peripheral vascular disease, diabetes, preexisting renal failure, COPD, preoperative ejection fraction, left main stenosis, number of diseased vessels, and urgent or emergency priority at operation. These variables are related to operative mortality and other adverse outcomes after CABG operation and have been suggested for risk adjustment of in-hospital CABG outcomes [10] and the American College of Cardiology/American Heart Association practice guidelines [11]. Operative variables included in the analysis were the use of bilateral ITA and the use of partial aortic clamps. Results of logistic regression were expressed as odds ratio with associated 95% confidence interval limits and *P* values. All analyses were performed by SPSS 11 software (SPSS Inc, Chicago, IL, USA).

Results

There were 100 MIDCAB and 900 OPCAB procedures performed during the data collection period. The distribution of single-vessel and multiple-graft OPCAB was 133 (14.7%) and 767 (85.2%) respectively. Of the latter subgroup, off-pump multiple grafting on the displaced beating heart was performed in 700 patients (91.2%). In 76 patients revascularization of the anterior wall was performed by sequential grafting of the left ITA to the LAD and diagonal arteries. Preoperative characteristics are listed in Table 1. The type of grafts and their distribution are illustrated in Figure 1.

IABP = intraaortic balloon pump
ITA = internal thoracic artery

RA = radial artery
RGEA = right gastroepiploic artery
COPD = chronic obstructive pulmonary disease
LAD = left anterior descending artery

Table 1. Preoperative characteristics

Variable	Single-vessel OPCAB (n=133)	Multiple-vessel OPCAB (n=767)	MIDCAB (n=100)
Age (yrs)			
Mean	66.7 ± 10.9	67.8 ± 11.2	64.8 ± 10.1
Range	34–91	56–95	37–93
Age ⩾ 80 yrs	18 (13.5)	165 (21.5)	12
Female gender	34 (25.5)	343 (44.7)	26
Hypertension	74 (55.6)	493 (64.3)	44
Diabetes mellitus	47 (35.3)	297 (38.7)	24
Peripheral vascular disease	23 (17.2)	141 (18.4)	6
Creatinine >2 mg/dl	19 (14.2)	67 (8.7)	5
Chronic lung disease	10 (7.5)	69 (8.9)	5
Acute MI (<1 week)	20 (15)	68 (8.8)	10
Congestive heart failure	36 (27.1)	126 (16.4)	8
Left main stenosis (>50%)	17 (12.7)	214 (27.9)	10
Triple-vessel disease	52 (39.1)	733 (95.5)	19
Ejection fraction ⩽ 35%	46 (34.6)	62 (8.1)	5
Emergency operation	14 (10.5)	55 (7.1)	0
Preoperative IABP	11 (8.2)	43 (5.6)	0
Prior cerebrovascular disease	20 (15)	71 (9.2)	5

Variables are expressed as n (%).
MI = myocardial infarction, IABP = intraaortic balloon pump, OPCAB = off-pump coronary artery bypass, MIDCAB = minimally invasive direct coronary artery bypass.

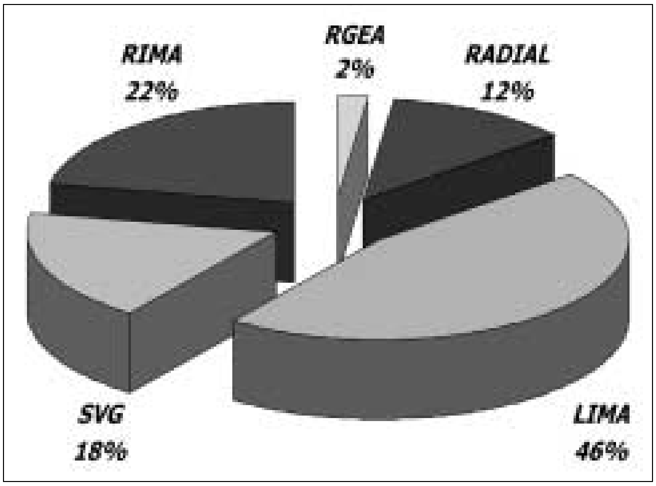

Figure 1. The type of conduits used during OPCAB. RIMA = right internal mammary artery, RGEA = right gastroepiploic artery, LIMA = left internal mammary artery, SVG = saphenous vein graft.

Table 3. Early results

	Single-vessel OPCAB (n=133)	Multiple-vessel OPCAB (n=767)	MIDCAB (n=100)
Length of hospital stay (days)			
Mean	4.9 ± 4.2	5.6 ± 4.4	4.5 ± 3.9
Range	2–21	3–30	2–15
30 day mortality	7 (5.2)	16 (2)	1
Myocardial infarction	3 (2.2)	10 (1.3)	0
Perioperative stroke	0	7 (0.9)	2
Sternal infection deep	0	12 (1.5)	0
Superficial	2 (1.5)	7 (0.9)	0
Renal failure*	5 (3.7)	34 (4.4)	1
Re-exploration d/t bleeding	2 (1.5)	10 (1.5)	1

Variables are expressed as n (%).
* Defined as serum creatinine level of 2 mg/dl or more or and postoperative increase of 1 mg/dl.

In the 700 patient multiple-vessel OPCAB subgroup the mean number of grafts per patients was 2.6 ± 0.6 (range 2–4). The type of grafts and their corresponding target vessels are listed in Table 2. Complete arterial revascularization was performed in 429 patients (61%) by *in situ* (65%) or T-graft configurations (35%). Arterial conduits, i.e., bilateral ITA, RAs and RGEAs, were used in 319 (45.5%), 182 (26%) and 28 (4%) patients, respectively, and saphenous vein grafts were used in 266 (38%). The number of anastomoses performed to the LAD, diagonal arteries, circumflex marginal arteries, right coronary arteries and posterior descending arteries were 700 (40%), 159 (9.1%) 510 (29.1%), 65 (3.7%) and 315 (18%), respectively. Subsequently, grafting of the postero-lateral territory was performed in 89% of these patients. Overall, 234 (31%) sequential anastomoses were performed; of these, 188 (26.8%) were performed on the postero-lateral aspect of the heart. Revascularization was complete in 96% and 69% in the multivessel and MIDCAB groups.

Overall early results (in-hospital and/or outcome within 30 days of the operation) are listed in Table 3. The predicted risk of early mortality was calculated using the Euroscore logistic model. This overall measure of predicted mortality was 4.8% and 8.3% in the multi- and single-vessel OPCAB groups, respectively. The observed mortality is presented in Table 3. The respective rates for perioperative stroke, perioperative myocardial infection and deep sternal wound infection in the multivessel group were 1%, 1.5%, and 0.7%. Logistic regression analysis identified preexisting renal dysfunction (creatinine serum level 2 mg/dl or more) (OR 11.5, CL 3.02–43.8; $P < 0.0001$) and emergency operation (OR 8.74, CL 1.99–38.3; $P = 0.004$) as predictors of early mortality in these patients.

Table 2. Multiple-vessel OPCAB subgroup: conduits used and the corresponding target coronary vessels

	Left internal thoracic artery	Right internal thoracic artery	Radial artery	Gastroepiploic artery	Saphenous vein graft
LAD	482 (27.1)	218 (12.3)	0	0	0
Diagonal	74 (4.2)	22 (1.2)	53 (2.9)	0	13 (0.7)
Circumflex marginal	211 (11.8)	93 (5.2)	154 (8.7)	0	87 (4.9)
Right coronary artery	0	11 (0.6)	27 (1.5)	0	34 (1.9)
Posterior descending artery	4 (0.2)	5 (0.3)	105 (5.9)	24 (1.4)	160 (9)

Variables are expressed as n (%)

Discussion

The patient subsets that are currently referred for CABG are associated with increased severity of disease and risk of poor outcomes

[1]. Conventional on-pump CABG is well established in the therapeutic armamentarium for treating ischemic heart disease, however several drawbacks exist. Embolic dislodgement of atherosclerotic plaques during surgical aortic manipulations, which may lead to embolic stroke, is among the most severe [12,13]. Off-pump coronary artery bypass obviates the need for aortic cannulation and cross-clamping and offsets untoward effects, such as inflammatory responses [14] and aerial or platelet aggregate emboli, related to the cardiopulmonary bypass. Recent advances in retractor-stabilizer systems and techniques of exposure of all surfaces of the heart have resulted in increased interest and acceptance of multivessel off-pump procedures. However, the construction of coronary anastomoses on the beating heart is technically demanding; subsequently, the feasibility of adopting this policy non-selectively (by all surgeons) remains unclear. This observational study presents the initial experience of a single center in Israel and adds to the growing body of knowledge documenting the safety and efficacy of off-pump procedures.

This analysis focused on the results of the multiple-graft OPCAB performed in patients with multivessel disease. This is the most technically challenging patient subset, in whom access to posterolateral coronary segments is required on the displaced beating heart. The high rate of complete revascularization (96%) was achieved despite wide variations in the individual surgeon's experience with OPCAB. Analysis of the effect of the individual surgeon's experience on the number of grafts performed is beyond the scope of this study; however, it is recognized that the gap in the number of grafts in comparison to on-pump CABG may be narrowing as operators gain more experience [2]. Concerning the choice of conduits and grafting configuration, the strategy we adopted was originally applied during on-pump CABG. The use of T-grafts or *in situ* configurations composed of skeletonized bilateral ITA, RA, or RGEA in these settings is associated with several advantages [9]. The benefits of arterial conduits, in terms of improved graft patency, event-free survival and survival, have been previously established [15]. Moreover, the use of these configurations in OPCAB settings allows complete myocardial revascularization without any aortic manipulation (no-touch technique) and is therefore particularly attractive in high risk patient subsets for atheromatous ascending aorta disease and subsequent atheroembolic stroke [16]. In addition, a technical advantage is conferred by *in situ* and T-grafts constructed prior to the performance of distal anastomosis. This allows progressive provision of coronary blood flow after completion of each distal anastomosis, in contrast to the more commonly used technique in which all distal saphenous vein graft anastomoses are performed prior to the proximal ones, thereby exposing the vulnerable beating heart to longer periods of ischemia.

Short-term safety after OPCAB has been a consistent finding [1,3]. The results of this study are compatible with those reported by other authors [3,4,6,8,17–19]. It is plausible that OPCAB would result in lower rates of atrial fibrillation and shorter lengths of hospital stay. Cardiopulmonary bypass has been recognized as one of the primary causes of the systemic inflammatory response that occurs after CABG operation and may contribute to multiple-organ dysfunction and postoperative complications. Avoidance of cardiopulmonary bypass during coronary artery operation is believed to reduce the inflammatory response. In a study by Matata and colleagues [14] comparing on-pump CABG with OPCAB, there were lower levels of oxidative stress, as measured by blood levels of lipid hydroperoxidases, protein carbonyls and nitrotyrosine, and less systematic inflammatory response among OPCAB patients. A study by Wan et al. [20] showed reduced cytokine response, especially interleukin-8 and interleukin-10 and lower postoperative levels of troponin-I among OPCAB patients.

The observed 5.2% mortality rate in the single-vessel OPCAB group should be viewed in face of the 8.3% expected mortality (logistic predicted mortality Euroscore model) in these subsets. This group includes very high risk patients who are intentionally referred to limited salvage surgery with prospects of future hybrid procedures [Tables 1 and 3].

Off-pump coronary artery bypass, however, is not without limitations. Despite improvements in current retractor-stabilizer systems, there is still some motion at the point of anastomosis, rendering the anastomosis associated with OPCAB technically more difficult. The surgeon and anesthesiologist must develop the ability to access all areas of the heart without causing hemodynamic derangement. In usual clinical practice most patients do not receive postoperative coronary angiography so there is no obvious method to assess the quality of the distal anastomoses. Nevertheless, techniques of quality control after off-pump coronary anastomoses have recently been introduced. It is our policy to systematically assess post-anastomosis patency by transit-time doppler flow measurements (Medi-Systems AS, Norway).

Several limitations of this observational study should be addressed. With respect to the evaluation of OPCAB procedures, this study examined only the short-term outcomes of the operation. Also, propensity-adjusted comparison with on-pump CABG patients is required to confirm these potential benefits of OPCAB operations.

In conclusion, the use of the OPCAB technique does not compromise the ability to achieve complete myocardial revascularization. Our procedure of choice is therefore the combination of OPCAB, multiple arterial grafts and 'no-touch' aorta techniques.

References

1. Disch DL, O'Connor GT, Birkmeyer JD, Olmstead EM, Levy DG, Plume SK. Changes in patients undergoing coronary artery bypass grafting: 1987–1990. Northern New England Cardiovascular Disease Study Group. *Ann Thorac Surg* 1994;57:416–23.
2. Hart JC, Spooner TH, Pym J, et al. A review of 1,582 consecutive Octopus off-pump coronary artery bypass patients. *Ann Thorac Surg* 2000;70:1017–20.
3. Arom KV, Flavin TF, Emery RW, Kshettry VR, Janey PA, Petersen RJ. Safety and efficacy of off-pump coronary artery bypass grafting. *Ann Thorac Surg* 2000;69:704–10.
4. Arom KV, Flavin TF, Emery RW, Kshettry VR, Petersen RJ, Janey PA. Is low ejection fraction safe for off-pump coronary artery bypass operation? *Ann Thorac Surg* 2000;70:1021–5.
5. Locker C, Shapira I, Paz Y, et al. Emergency myocardial revascularization for acute myocardial infarction: survival benefits of avoiding cardiopulmonary bypass. *Eur J Cardiothorac Surg* 2000;17:234–8.

6. Koutlas TC, Elbeery JR, Williams JM, Moran JF, Francalancia NA, Chitwood R. Myocardial revascularization in the elderly using beating heart coronary artery bypass surgery. *Ann Thorac Surg* 2000;69:1042–7.
7. Hernandez F, Clough RA, Klemperer JD, Blum JM. Off-pump coronary artery bypass grafting: initial experience at one community hospital. *Ann Thorac Surg* 2000;70:1070–2.
8. Kshettry VR, Flavin TF, Emery RW, Nicoloff DM, Arom KV, Petersen RJ. Does multivessel, off-pump coronary artery bypass reduce postoperative morbidity? *Ann Thorac Surg* 2000;69:1725–31.
9. Lev-Ran O, Paz Y, Pevni D, et al. Bilateral internal thoracic artery grafting: midterm results of composite versus in-situ crossover graft. *Ann Thorac Surg* 2002;74:704–11.
10. Hosmer D, Lemeshow S. Applied Logistic Regression. New York: John Wiley & Sons, 1989.
11. Jones RH, Hannan EL, Hammermeister KE, et al. Identification of preoperative variables needed for risk adjustment of short-term mortality after coronary artery bypass graft surgery. *J Am Coll Cardiol* 1996;28:1478–87.
12. Roach GW, Kamchuger M, Mangano CM, et al. Adverse cerebral outcome after coronary bypass surgery. *N Engl J Med* 1996;335:1857–64.
13. Barbut D, Yao FF, Lo YW, et al. Determination of size of aortic emboli and embolic load during coronary artery bypass. *Ann Thorac* 1997;63:1262–7.
14. Matata BM, Sosnowski AW, Gilnanes M. Off-pump bypass graft operation significantly reduces oxidative stress and inflammation. *Ann Thorac Surg* 2000;69:785–91.
15. Taggart DP, D'Amico R, Altman DG. Effect of arterial revascularization on survival: a systematic review of studies comparing bilateral and single internal mammary arteries. *Lancet* 2001;358:870–5.
16. Lev-Ran O, Loberman D, Matsa M, et al. Reduced strokes in the elderly: the benefits of untouched aorta off-pump coronary surgery. *Ann Thorac Surg* 2004;77:102–7.
17. Ascione R, Lloyd CT, Underwood MJ, Lotto A, Pitsis AA, Angelini GD. Economic outcome of off-pump coronary artery bypass surgery: a prospective randomized study. *Ann Thorac Surg* 1999;68:2237–42.
18. Puskas JD, Thourani VH, Marshall JJ, et al. Clinical outcomes, angiographic patency, and resource utilization in 200 consecutive off-pump coronary bypass patients. *Ann Thorac Surg* 2001;71:1477–84.
19. Yokoyama T, Baumgartner FJ, Ghiessari A, et al. Off-pump versus on-pump coronary bypass in high-risk subgroups. *Ann Thorac Surg* 2000;70:1546–50.
20. Wan S, Izzat MB, Lee TW, et al. Avoiding cardiopulmonary bypass in multivessel CABG reduces cytokine response and myocardial injury. *Ann Thorac Surg* 1999;68:52–7.

Correspondence: Dr. O. Lev-Ran, Dept. of Cardiothoracic Surgery, Tel Aviv Sourasky Medical Center, 6 Weizmann Street, Tel Aviv 64239, Israel.
Phone: (972-3) 692-3322
Fax: (972-3) 627-4439
email: orenlevran@hotmail.com, levran@tasmc.health.gov.il

Capsule

Tumor cells staying alive in spite of Gefitinib

About 10% of patients with non-small cell lung cancer (NSCLC) experience dramatic tumor regression when treated with Gefitinib (Iressa), a recently approved drug that inhibits the kinase activity of the epidermal growth factor receptor (EGFR). Tumors that respond to Gefitinib harbor somatic mutations in the EGFR kinase domain. Sordella et al. show that these mutant EGFRs activate a signaling pathway that keeps the tumor cells alive even when they are treated with agents that induce cell death, such as conventional chemotherapeutic drugs. The authors speculate that NSCLCs expressing the mutant EGFRs may become fully dependent on this cell survival pathway, which could explain, at least in part, their extreme sensitivity to Gefitinib.

Science 2004;305:1163

E. Israeli

Capsule

Clearing a respiratory virus

Moyron-Quiroz et al. show that a distinct lymphoid tissue that forms locally at the site of infection contributes to clearing a respiratory virus. In mice engineered to lack lymph nodes and spleen (SLP mice), the appearance of activated B and T lymphocytes in response to influenza virus infection was found to be delayed but not otherwise impaired. Histologic examination of lungs from these infected mice revealed sites with induced bronchus-associated lymphoid tissue (iBALT). Although the pathways leading to iBALT formation appeared distinct from those involved in the development of conventional lymphoid tissue, these sites possessed organized regions of proliferating T and B cells equivalent to those normally found in lymph nodes and spleen. Furthermore, SLP mice cleared virus efficiently and with reduced immune pathology, suggesting that iBALT may support locally efficient pathogen clearance while minimizing the global cost of a systemic immune reaction.

Nature Med 2004;10.1038/nm1091

E. Israeli